i supplementi di

tumori

a Journal of Experimental and Clinical Oncology

Bimestrale - Sped. Abb. Post. - 45% - Art. 2 Comma 20B Legge 662/96 - Filiale di Roma.

Volume 11, Number 2, October 2011

***i supplementi* di TUMORI,** a Journal of Experimental and Clinical Oncology
a publication of Fondazione IRCCS Istituto Nazionale dei Tumori, Milan (Marco A. Pierotti, Director)
an Official Journal of Società Italiana di Cancerologia (Alfredo Fusco, President)
Associazione Italiana di Oncologia Medica (Carmelo Iacono, President)
Società Italiana di Chirurgia Oncologica (Francesco Tonelli, President)
and Associazione Italiana di Radioterapia Oncologica (Enza Barbieri, President)

Editorial Assistants: Elena Morittu, Betty Johnston, Laura Zanesi, Marije de Jager.
Editorial Office: Fondazione IRCCS Istituto Nazionale dei Tumori, via Venezian 1, 20133 Milan, Italy.
Tel +39-02-23902291 - Fax +39-02-23902195. *E-mail:* tumori@istitutotumori.mi.it *Internet:* www.istitutotumori.mi.it

Tumori is published for the "Fondazione IRCCS Istituto Nazionale dei Tumori" by Il Pensiero Scientifico Editore, via San Giovanni Valdarno 8, 00138 Roma. E-mail: pensiero@pensiero.it
Internet: www.tumorionline.it
Production Mara Losi and Arabella Festa; *Advertising* Maria Nardoianni, Tiziana Tucci; *Subscriptions* Andrea De Fiore.

Direttore Responsabile: Marco A. Pierotti. Autorizzazione del Tribunale di Milano in data 18 ottobre 1948 n. 704 del Registro. Periodicità bimestrale. Finito di stampare nel mese di ottobre 2011 dalle Arti Grafiche Tris srl - 00131 Roma - Via delle Case Rosse, 23. Tel 06/41294630.

2011 Iscritto all'Unione Stampa Periodica Italiana

***i supplementi di* TUMORI**, a Journal of Experimental and Clinical Oncology
Volume 11, Number 2, October 2011

XIII NATIONAL CONGRESS OF MEDICAL ONCOLOGY

November 5-7, 2011: Bologna, Italy

Guest Editor

Carmelo Iacono
Director, Department of Oncology, ASP 7 Ragusa
President, Italian Association of Medical Oncology (AIOM)

Il Pensiero Scientifico Editore

The Scientific Committee has chosen the papers on the basis of the originality of the research and the originality of the results. The authors are responsible for the text and the translation.

***i supplementi di* TUMORI**, a Journal of Experimental and Clinical Oncology
Volume 11, Number 2, October 2011

CONTENTS
(indexed in Current Contents/Life Sciences, EMBASE/Excerpta Medica, Elsevier BIOBASE/Current Awareness in Biological Sciences)

XIII NATIONAL CONGRESS OF MEDICAL ONCOLOGY

November 5-7, 2011: Bologna, Italy

Abstracts

Please, note that abstracts marked with an asterisk (*) are Oral communications.

13th National Congress of Medical Oncology
November 5-7, 2011: Bologna, Italy

Guest Editor
Carmelo Iacono
Director, Department of Oncology, ASP 7 Ragusa
President, Italian Association of Medical Oncology (AIOM)

The management of cancer patients has become increasingly complex and multidisciplinary, strongly calling for more professional skills by medical oncologists. These range from an understanding of the new aspects of molecular diagnostics and their implications for treatment decision making to new imaging techniques and the essential ability to work together with a multitude of other specialists (pathologists, radiologists, surgeons, radiotherapists, geriatricians, etc.) when planning strategies for therapeutic interventions.

These changes involve all aspects of overall patient care, with the medical oncologist being responsible for handling any complications that may come up during the course of the disease. This has led us to look at the patient from different standpoints, giving due importance to a multidimensional view which takes into account all the physical, functional, psychological, social and spiritual needs of patients and their families. From a professional standpoint, this aspect complicates the task of the medical oncologist, because appropriate training in communication is obviously required.

The new medical oncologist needs to establish a sincere and true relationship with patients and their families, given that patients will be followed for the rest of their lives in a complicate cycle, with the doctor being the managing reference for all issues that will come up. The increasing value given to support and patients' overall daily needs is just a part of the complex role of health care in general, and is one of the main aspects of modern medicine and the fascinating advances deriving from biomolecular medicine. Medical humanization requires modern skills in cultural and scientific growth as well as in health care in general, including profound knowledge of palliative care and management. A professional capability to address all patient requirements in the most appropriate, safe and efficient way is warranted.

This model of simultaneous care has been addressed by the Italian Association of Medical Oncology (AIOM) ever since its foundation in 1973, together with encouragement in improving the cultural imprinting and professional skills of medical oncologists. The process has required a close and positive relationship with other scientific societies such as the European Society for Medical Oncology (ESMO), in order to generate common educational tools and a common approach to matters not strictly related to cancer, such as social and ethical issues. These topics will all be discussed during the 13th AIOM National Congress, providing a broader view of medical oncology, not restricted to anticancer treatment but open to interactions with different areas including prevention, screening, translational research, palliative care, organizational aspects, ethics, and multidisciplinary approaches. The proceedings of the congress are published in this special issue of *Tumori*.

On behalf of all members of the Scientific Board, I declare that the Bologna congress will provide a rich and fruitful opportunity for medical oncologists to widen their expertise and skills, and will give them a chance to share their ideas on scientific and health-care issues at the highest level. Delegates will have the added opportunity to exchange knowledge with colleagues who, thanks to experience abroad, are able to put the topics of the meeting into a different cultural perspective and discuss different dimensions.

The Board of Directors for the years 2009-2011 includes:

- Carmelo Iacono (President)
- Marco Venturini (*President Elect*)
- Giovanni Bernardo (Secretary)
- Maria Teresa Ionta (Treasurer)
- Massimo Aglietta
- Roberto Bordonaro
- Paolo Carlini
- Giovanni Condemi
- Stefania Gori
- Paolo Marchetti
- Carmine Pinto
- Valter Torri

We are looking forward to seeing you in Bologna.

Dr. Carmelo Iacono
(President of the Congress)

This abstracts book will be available on-line and will also be freely available to all visitors to the following website from Novembr 8th, 2011 (http://www.aiom.it/default.asp)

Plenary session

1* ERLOTINIB VS CHEMOTHERAPY (CT) IN ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS (PTS) WITH EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) ACTIVATING MUTATIONS: THE EURTAC PHASE III RANDOMIZED TRIAL INTERIM RESULTS

de Marinis F.[1], Rosell R.[2], Vergnenegre A.[3], Di Seri M.[4], Illiano A.[5], Milella M.[6], Altavilla G.[7], Gebbia V.[8], Bearz A.[9], Cortesi E.[4], Farris A.[10], Tagliaferri P.[11], Longo F.[4], Battiloro C.[5], Ricciardi S.[1], Paz-Ares L.[12]

[1]San Camillo-Forlanini Hospitals, Rome; [2]Germans Trias i Pujol Hospital, Badalona (Barcelona, Spain); [3]Cluzeau Hospital, Limoges (France); [4]Umberto I University Hospital, Rome; [5]Monaldi Hospital, Naples; [6]Regina Elena Institute, Rome; [7]G. Martino University Hospital, Messina; [8]P. Giaccone University Hospital, Palermo; [9]CRO, Aviano; [10]SS. Annunziata Hospital, Sassari; [11]Materdomini University Hospital, Cosenza; [12]Virgen del Rocio University Hospital, Seville (Spain)

Background. EGFR tyrosine kinase activating mutations are present in 10-26% of NSCLC tumours and are associated with increased response to gefitinib and erlotinib. However, little is known about how the efficacy and safety profile of erlotinib compares with CT in EGFR-mutant Caucasian patients. The Spanish Lung Cancer Group has performed the European Tarceva® vs Chemotherapy (EURTAC) phase III randomized trial comparing erlotinib with platinum-based CT in chemo-naïve advanced NSCLC pts with EGFR mutations.

Material and methods. From February 2007 to January 2011, we screened 1275 pts from 42 centers in Spain, France and Italy for EGFR mutations, and 154 pts were randomly assigned to receive erlotinib or platinum-based CT. The primary endpoint was progression-free survival (PFS). Secondary endpoints included response, overall survival and toxicity profiles. Investigator-assessed PFS and response were reviewed by an independent review committee.

Results. Accrual is now complete. Fifty-five pts have died, 2 pts were lost to follow-up and 97 pts remain on study. 153 pts (76 CT, 77 erlotinib) are evaluable for the interim analysis. Patients characteristics CT arm: 16 males; median age, 64; never smokers, 56; PS 0, 26; PS 1, 41; adenocarcinoma, 67. Patients characteristics erlotinib arm: 25 males; median age, 65; never smokers, 54; PS 0, 23; PS 1, 44; adenocarcinoma, 73. Preliminary results of the interim analysis are now available. Response rate was 10.5% to CT vs 54.5% to erlotinib ($p < 0.0001$). PFS in the CT arm was 5.2 months (m) (95% CI, 4.4-5.8 m) compared to 9.4 m (95% CI, 7.9-12.3) in the erlotinib arm (HR, 0.42; $p < 0.0001$). Median survival was 18.8 m in the CT arm and 22.9 m in the erlotinib arm (HR, 0.80; $p = 0.42$). Most common toxicities were asthenia (68.9%), anemia (45.9%), nausea (40.5%) and neutropenia (36.5%) in the CT arm, and diarrhea (57.3%), asthenia (53.3%), and rash (49.3%) in the erlotinib arm. Final results of the interim analysis will be presented.

Conclusions. The EURTAC study met its primary endpoint at the interim analysis. Erlotinib as first-line treatment for advanced NSCLC pts with EGFR mutations improves PFS, with acceptable toxicity, compared to platinum-based chemotherapy.

2* PARAMOUNT: PHASE III STUDY OF MAINTENANCE PEMETREXED PLUS BEST SUPPORTIVE CARE VERSUS PLACEBO PLUS BEST SUPPORTIVE CARE FOLLOWING INDUCTION TREATMENT WITH PEMETREXED PLUS CISPLATIN FOR ADVANCED NON-SQUAMOUS NON-SMALL CELL LUNG CANCER (NSCLC)

Gridelli C.[1], de Marinis F.[2], Dediu M.[3], Thomas M.[4], Pujol J.L.[5], Bidoli P.[6], Molinier O.[7], Laack E.[8], Reck M.[9], Chella A.[10], Amoroso D.[11], Fasola G.[12], Bearz A.[13], Boni C.[14], Grossi F.[15], Maione P.[1], Ricciardi S.[2], Cortinovis D.[6], Corral J.[16], Melemed S.[17], John W.[17], Chouaki N.[18], Zimmermann A.[17], Visseren-Grul C.[19], Paz-Ares L.[16]

[1]San G. Moscati Hospital, Avellino; [2]San Camillo-Forlanini Hospitals, Rome; [3]Institute of Oncology, Bucharest, Romania; [4]Thoraxklinik, University Heidelberg, Heidelberg, Germany; [5]Montpellier Academic Hospital, Montpellier, France; [6]San Gerardo Hospital, Monza; [7]Le Mans Regional Hospital, Le Mans, France; [8]University Hospital Hamburg-Eppendorf, Germany; [9]Hospital Grosshansdorf, Grosshansdorf, Germany; [10]Cisanello Hospital, Pisa; [11]Lido di Camaiore Hospital, Viareggio; [12]S. Maria della Misericordia Hospital, Udine; [13]CRO, Aviano; [14]Arcispedale S. Maria Nuova, Reggio Emilia; [15]IST, Genova; [16]Virgen del Rocio University Hospital, Seville, (Spain); [17]Eli Lilly and Company, Indianapolis, IN, USA; [18]Eli Lilly and Company, Suresnes, Hauts de Seine, France; [19]Eli Lilly and Company, Houten, The Netherlands

Purpose. The PARAMOUNT trial investigated whether pemetrexed continuation maintenance improves progression-free survival (PFS) after pemetrexed-cisplatin induction therapy in patients with advanced non-squamous NSCLC.

Methods. In this double-blind, placebo-controlled trial, 939 patients (175 from the Italian Centers) participated in the induction phase: four cycles of induction pemetrexed (500 mg/m^2) plus cisplatin (75 mg/m^2) on day 1 of a 21-day cycle. Patients who had not progressed after induction and had a performance status of 0/1 (n = 539, 57.4%) were randomized (2:1) to continuation maintenance pemetrexed (500 mg/m^2 on day 1 of a 21-day cycle) plus best supportive care (BSC) (n = 359) or placebo plus BSC (n = 180) until disease progression. The primary endpoint was PFS.

Results. The study met its primary endpoint as treatment with pemetrexed continuation maintenance resulted in a 36% reduction in the risk of disease progression over the placebo maintenance arm (HR = 0.64; 95% CI: 0.51-0.81; $p = 0.00025$). The median independently reviewed PFS (472 patients), measured from randomization, was 3.9 months (95% CI: 3.0-4.2) for pemetrexed and 2.6 months (95% CI: 2.2-2.9) for placebo. The disease control rate measured from randomization was 72% for pemetrexed and 60% for placebo ($p = 0.009$). The pemetrexed arm had a higher incidence of possibly treatment-related grade 3/4 laboratory adverse events (AEs) (9% pemetrexed, 0.6% placebo; $p < 0.001$) and grade 3/4/5 non-laboratory AEs (9% pemetrexed, 4% placebo; $p = 0.080$, with one death reported on each arm). Discontinuations due to AEs were 9% for pemetrexed and 4% for placebo.

Conclusions. Pemetrexed continuation maintenance following pemetrexed-cisplatin induction is an effective and well tolerated treatment for patients with advanced non-squamous NSCLC.

3* ETOPOSIDE, DOXORUBICIN, CISPLATIN, AND MITOTANE VERSUS STREPTOZOTOCIN AND MITOTANE IN ADRENOCORTICAL CARCINOMA. PRELIMINARY RESULTS FROM THE FIRST INTERNATIONAL PHASE III TRIAL "THE FIRM-ACT STUDY"

Sperone P.*, Fassnacht M.°, Terzolo M.**, Allolio B.°, Baudin E.^, Haak H.°°, Berruti A.*, Mueller H.H.°, Skogseid B.§ on behalf of the FIRM-ACT investigators

**Department of Medical Oncology, University of Turin, Hospital San Luigi, Orbassano, Italy; °Department of Internal Medicine I, Endocrine and Diabetes Unit, University Hospital of Würzburg, Germany; **Department of Internal Medicine I, University of Turin, Hospital San Luigi, Orbassano, Italy; ^Department of Nuclear Medicine and Endocrine Oncology, Institut Gustave Roussy, Villejuif, France; °°University Medical Centre, Leiden, The Netherlands; §University Department of Medical Sciences, Uppsala University, Sweden*

Background. No randomized trials have been conducted in adrenocortical carcinoma (ACC) patients. Treatment recommendations for this rare but aggressive disease have been based on data from small phase II trials. We have now performed the first randomized phase III trial, comparing etoposide, doxorubicin, cisplatin plus mitotane (EDP-M) against streptozotocin plus mitotane (Sz-M).

Methods. Three-hundred and four chemotherapy-naïve patients with ACC not amenable to radical surgery were randomly assigned to receive either EDP-M or Sz-M until progression. In case of progression, the alternative regimen was offered to the patient. The primary endpoint was overall survival. Key secondary endpoints were time to progression and response to second-line therapy.

Results. 151 patients randomized to EDP-M as first-line treatment received 608 cycles (scheduled every 28 days) and 153 patients in the Sz-M group 634 cycles (every 21 days). Forty-seven patients experienced 87 serious adverse events (SAE) during first-line treatment with EDP-M in comparison with 37 patients with 68 SAEs in the Sz-M group ($p = 0.199$). Median overall survival in the EDP-M and Sz-M groups (107 and 124 deaths, respectively) were 14.8 and 12.0 months, respectively (HR 0.79, 95% CI, 0.61 to 1.02, $p = 0.069$). Median time to progression was 5.0 vs 2.1 months (HR 0.54, 95% CI 0.42 to 0.68, $p < 0.0001$). Patients treated with EDP-M after failure of Sz-M ($n = 83$) had a median time to progression of 6.2 months. In contrast, time to progression in 75 patients treated with Sz-M as second-line was only 2.1 months. In both groups, patients pre-treated with mitotane had a similar outcome compared to mitotane-naïve patients.

Conclusions. Although a trend towards better overall survival in patients with advanced ACC treated with EDP-M as first-line therapy was observed, overall survival was not significantly different between groups. However, EDP-M significantly prolonged time to tumour progression compared with Sz-M. Thus, new treatment regimens for advanced ACC should be tested against EDP-M.

4* BONE EFFECTS OF ADJUVANT TAMOXIFEN (T), LETROZOLE (L) OR L + ZOLEDRONIC ACID (Z) IN EARLY BREAST CANCER (EBC). THE PHASE 3 HOBOE STUDY

Nuzzo F.[1], Signoriello S.[2], Lastoria S.[1], Gravina A.[1], Landi G.[1], Rossi E.[1], Pacilio C.[1], Labonia V.[1], Di Rella F.[1], De Laurentiis M.[1], Bartiromo A.[1], Piccirillo M.C.[1], Di Maio M.[1], Giordano P.[1], Daniele G.[1], De Feo G.[1], Buonfanti G.[1], Esposito G.[1], Gallo C.[2], de Matteis A.[1], Perrone F.[1]

[1]National Cancer Institute, Napoli; [2]Second University of Napoli

Background. Treatment with L can reduce bone mineral density (BMD) in patients (pts) with EBC. However, the addition of Z may protect against bone loss.

Patients and methods. We performed a 1:1:1 randomized phase 3 trial to compare the bone effects of adjuvant T, L or L+Z in pre- and postmenopausal pts with hormone-receptor positive EBC. Premenopausal pts also received triptorelin. Primary endpoint was T-score at lumbar spine (LST) measured by DXA-scan 1 year after randomization. The study had 80% power to detect a 0.35 effect size. Two comparisons were planned: L vs T and L+Z vs L; for each one, a linear model was applied to test treatment effect adjusted by age, menopausal status, previous chemotherapy and baseline LST. Two exploratory analyses were done to test whether baseline body mass index (BMI) and 6-month estradiol level were associated with L vs T effect. NCT00412022

Results. From March '04 to December '09, 483 patients were enrolled; 459 (247 pre- and 212 postmenopausal) were available for primary analyses. Median age was 50 (range 28-80); 320 (70%) pts had received adjuvant chemotherapy. At baseline 35%/23% of the pts were overweight/obese. At 1-year, mean (SD) change of LST from baseline was -0.27 (0.64) with T, -0.57 (0.66) with L and +0.02 (0.59) with L+Z. Both L vs T and L+Z vs L comparisons were highly statistically significant, $p < 0.0001$. In premenopausal pts, but not in postmenopausal ones, bone effect of L (vs T) decreased with increasing values of baseline BMI (interaction test $p = 0.004$ and $p = 0.47$, respectively). There was no interaction between 6-month estradiol level and bone treatment effect, in both menopausal subgroups ($p = 0.31$ and $p = 0.22$, respectively).

Conclusions. The HOBOE study confirms that L decreases BMD as compared with T, and that the addition of Z protects against this side effect. Interestingly, BMI seems predictive of L effect on bone health among premenopausal but not postmenopausal pts; these findings are consistent with previous observations. HOBOE has been extended and is now recruiting only premenopausal pts, to test disease-free survival effects. Novartis kindly supplied Z (for all pts) and L (for premenopausal pts).

Partially supported by AIRC.

5* HER2 GENE COPY NUMBER GAIN IN CHEMO-REFRACTORY METASTATIC COLORECTAL CANCER (mCRC) PATIENTS TREATED WITH CETUXIMAB: RESULTS OF AN INTERNATIONAL CONSORTIUM

Martin V.[1], Sacconi A.[2], Landi L.[3], Riva A.[1], Saletti P.[4], De Dosso S.[4], Geva R.[5,6], Tejpar S.[5], Fountzilas G.[7], Kalogeras K.T.[7], Molinari F.[1], Mazzucchelli L.[1], Frattini M.[1], Cappuzzo F.[3]

[1]Laboratory of Molecular Diagnostic, Istituto Cantonale di Patologia, Locarno, Switzerland; [2]Italian National Cancer Institute "Regina Elena", Rome, Italy; [3]Department of Medical Oncology, Ospedale Civile di Livorno, Livorno, Italy; [4]Oncology Institute of Southern Switzerland, Ospedale San Giovanni, Bellinzona,

Switzerland; [5]Department of Digestive Oncology, University Hospital Gasthuisberg, K.U. Leuven, Leuven, Belgium; [6]Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel; [7]Hellenic Cooperative Oncology Group (HeCOG) Athens, Greece and Aristotle University of Thessaloniki School of Medicine, Thessaloniki, Greece

Introduction. KRAS mutation represents the only validated biomarker used in clinical practice for selection of metastatic colorectal cancer (mCRC) candidates for therapy with the anti-Epidermal Growth Factor Receptor (EGFR) monoclonal antibody cetuximab. Previous studies conducted in small cohorts of patients suggested that HER2, the major EGFR partner, could modify the sensitivity to anti-EGFR agents. Aim of the present study was to investigate the role of HER2 gene copy number in a cohort of mCRC patients treated with cetuximab.

Patients and methods. Chemorefractory mCRC patients treated with cetuximab alone or in combination with irinotecan were collected in an international consortium effort. HER2 gene status was analyzed using the dual-color FISH assay LSI HER2/neu-CEP17 (PATHVYSION, Abbott) in one central lab, whereas KRAS and BRAF mutations were investigated locally. For HER2 evaluation, we used the "Colorado score": cases were classified as positive when ≥4 copies of the gene in ≥40% of cells or gene amplification were observed, negative in the remaining cases. Log-rank and Chi-square tests were applied in the statistical analysis.

Results. Four hundred and seven patients were collected. Objective response rate (ORR) was observed in 25.3% of the patients. HER2 gene status was evaluable in 288 cases (70.8%). In HER2-positive cases (81 cases, 28.8%) response was observed in 34.6% of the patients (vs 15.7% in negative cases, $p < 0.001$), with an overall median progression-free survival (PFS) of 5.14 months (vs 3.0 months in negative cases, $p = 0.004$) and a median overall survival (OS) of 10.9 months (vs 9.8 months in negative cases, $p = 0.44$). KRAS and BRAF mutations are under investigation.

Conclusions. Data from this large retrospective study suggested that HER2 gene status evaluated by FISH might represent an additional marker useful for the identification of mCRC patients who might benefit from EGFR-targeted therapies. The interplay between EGFR and HER2 needs to be further investigated for future best-tailored treatments.

Session A • Breast cancers

A1* ADJUVANT TRASTUZUMAB (T) IN HER2-POSITIVE (HER2+) EARLY BREAST CANCER (EBC) AND CARDIOTOXICITY IN CLINICAL PRACTICE: RESULTS OF ICARO (ITALIAN CARDIO-ONCOLOGICAL) NETWORK

Tuccia F.[1], Capristo C.[2], Parisi A.M.[2], Giotta F.[3], De Laurentiis M.[4], Maurea N.[5], Oliva S.[6], Cioffi G.[7], Tarantini L.[8], Foglietta J.[9], Stocchi L.[9], Gori S.[9]

[1]Divisione Oncologia, Ospedale San Martino ASL 1, Belluno; [2]UO Patologia della mammella, AO San Camillo, Roma; [3]UO di Oncologia Medica e Sperimentale, IRCCS Giovanni Paolo II, Bari; [4]Oncologia Medica Senologica, Istituto Pascale, Napoli; [5]Cardiologia, Istituto Pascale, Napoli; [6]Cardiologia, IRCC S. Giovanni Paolo II, Bari; [7]Cardiologia, Villa Bianca, Trento; [8]Cardiologia, Ospedale San Martino ASL1, Belluno; [9]Oncologia Medica, Perugia

Background. Adjuvant trastuzumab therapy improved survival of HER2+EBC patients.

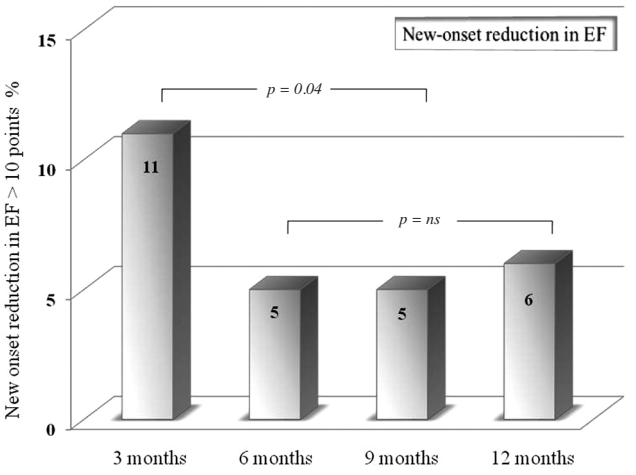
A careful monitoring of ventricular function is needed due to potential trastuzumab-cardiotoxicity.

To date, it is not well known the real incidence of adjuvant trastuzumab-cardiotoxicity in clinical practice due to criteria used to start T in real word and absence of uniform definition of cardiotoxicity in Randomized Clinical Trials (RCT).

Patients and methods. 499 consecutive HER2+EBC treated with trastuzumab between January 2008 and June 2009 at 10 Italian institutions. We evaluated incidence, time of occurrence, clinical features and predictive factors of cardiotoxicity in EBC patients treated with adjuvant trastuzumab. Cardiotoxicity was defined according to CTCAE-NCI-2.0 and NYHA Class. LVEF was evaluated by echocardiography at baseline and at 3-6-9-12 months during trastuzumab-therapy.

Results. Cardiotoxicity was reported in 133/499 patients (26.7%): 102 patients (20.4%) showed asymptomatic reduction of LVEF >10% but ≤20% (G1); 15 (3.0%) asymptomatic decline of LVEF >20% or below <50% (G2); 16 (3.2%) symptomatic CHF (G3). All patients with symptomatic CHF were in NYHA-Class II. Trastuzumab was discontinued due to cardiotoxicity in 20 patients (15%) and restarted in 9 (7%) after LVEF recovery. The most critical period for cardiotoxicity appearance was trastuzumab start (Figure 1). Cardiotoxicity developed in older patients (mean age ± DS: 57 ±11 yrs vs 55 ± 11; p <0.03), in patients with higher creatinine levels (0.86 ± 0.16 mg/dL vs 0.77 ± 0.14; p <0.003) and in patients pretreated with doxorubicin and radiotherapy. At multivariate analysis an impaired renal function (GFR <80 mL/min*1.73 m^2) (OR 3.19; 95% CI: 1.04-9.74, p <0.04) and doxorubicin exposure (3.16, 95% CI: 1.06-9.39, p <0.04) were independent predictors for cardiotoxicity development.

Conclusions. In clinical practice trastuzumab-cardiotoxicity is frequent in HER2+ EBC (133/499 patients = 26.4%). Cardiac damage is mild and clinically asymptomatic in the majority of patients. Nevertheless, cardiotoxicity causes trastuzumab interruption in about 6% patients, percentage higher than reported in RCT.



A2* NEOADIXERN-GIM9: A FEASIBILITY STUDY OF DOSE-DENSE (DD) FEC WITH G-CSF SUPPORT FOLLOWED BY DD IXABEPILONE WITH G-CSF SUPPORT AS NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER (BC)

Clavarezza M.[1], Bordonaro R.[2], Ferrandina G.[3], Daniele B.[4], Barni S.[5], De Laurentiis M.[6], Gravina A.[6], De Placido S.[7], Contu A.[8], Carrozza F.[9], Del Mastro L.[10], Cognetti F.[11], Venturini M.[1]

[1]Ospedale Sacro Cuore Don Calabria, Negrar (Vr); [2]Ospedale Vittorio Emanuele II, Catania; [3]Università Cattolica del Sacro Cuore, Campobasso; [4]Azienda Ospedaliera G. Rummo, Benevento; [4]Azienda Ospedaliera Treviglio-Caravaggio, Bergamo; [6]Istituto Nazionale Tumori Fondazione Pascale, Napoli; [7]Università Federico II, Napoli; [8]Ospedale Civile SS Annunziata, Sassari; [9]Ospedale A. Cardarelli, Campobasso; [10]Istituto Nazionale Ricerca Cancro, Genova; [11]Istituto Regina Elena, Roma

Background. DD chemotherapy is effective in ER- BC. Ixabepilone is an antimicrotubular agent effective in phase II-III previously treated metastatic BC. No data exist about DD ixabepilone.

Patients and methods. Endpoints: 1) feasibility of neoadjuvant DD ixabepilone; 2) pCR: absence of invasive carcinoma in breast and axilla. Treatment schedule: FEC 600/90/600 mg/m^2 DD with G-CSF support followed by ixabepilone 40 mg/m^2 DD with G-CSF support. Inclusion criteria: histological diagnosis of BC, ER-, tumor size >2 cm. Protocol was amended to include also ER+ BC because of low accrual. Definition of feasibility: absence of hematologic toxicity requiring dose reduction or treatment interruption (neutropenia grade 4 >7 days and/or febrile neutropenia, thrombocytopenia grade >3 with significant bleeding or requiring blood transfusion, thrombocytopenia grade 4) or any grade ≥3 non hematological toxicity, excluding alopecia, nausea/vomiting and bone pain. Toxicity was evaluated according to NCI-CTC 3.0. Statistical considerations: two steps Simon's design. First step: ≤5/20 non feasibility to continue enrollment of other 20 patients at the dose of 40 mg/m^2 of ixabepilone DD. If ixabepilone was not feasible in less than 7/40 patients the regimen was defined feasible. Evaluable patients: received at least one cycle of ixabepilone.

Results. Forty-seven enrolled patients: ER- 24/47 (51%), ER+ 23/47 (49%), HER2- 36/47 (77%), HER2+ 11/47 (23%). Forty-

three evaluable patients at the dose of ixabepilone 40 mg/m^2 DD; regimen was feasible for 32/43 (74%), not feasible for 11/43 (26%). Reasons of non feasibility: interruption: 6 patients (mucositis G3, astenia G3, neuropathy G3, febrile neutropenia, hepatotoxicity G3, consent withdrawal); dose reductions: 4 patients (neutropenia G4, neutropenia G2 of more than 7 days, neuropathy G3, neuropathy G2 >7 days), 1 toxic death. 4/47 patients not evaluable (4 interruptions during FEC: 2 because of toxicity and 2 consent withdrawal). Efficacy: 42/47 evaluable; pCR: 16/42 (38%); ER- 11/22 (50%), ER+ 5/20 (25%).

Conclusions. DD ixabepilone is not feasible at the dose of 40 mg/m^2. In ER- BC pCR rate was high (50%).

A3* DISCORDANCE IN PATHOLOGY REPORT AFTER CENTRAL PATHOLOGY REVIEW IN EARLY BREAST CANCER AND ITS IMPACT ON TREATMENT DECISION

Orlando L., Viale G.*, Schiavone P., Fedele P., Calvani N., Nacci A., Cinefra M., Mazzoni E., Marino A., Sponziello F., Rizzo P., D'Amico M., Chetrì C., Cinieri S.

*U.O. Oncologia Medica and Breast Unit, Senatore Antonio Perrino Hospital, ASL Brindisi; *U.O. Anatomia Patologica, Istituto Europeo di Oncologia, Università degli Studi, Milano*

Purpose. Systemic therapies in early breast cancer are chosen on the basis of predictive factors mainly defined by immunohistochemistry. In large clinical trials the rate of discordance between local and central pathologic assessment is noteworthy. In this retrospective analysis we evaluated the discordance rate in histological report and the clinical impact on treatment decision process, after central pathologic review of early breast cancer.

Methods. A retrospective pathology review was performed on formalin-fixed and paraffin-embedded tissue from primary breast cancers collected from different Italian Cancer Centers from 2008 to 2010, by the Central Pathology Laboratory at the European Institute of Oncology in Milan. Central review included assessment of histologic subtype, grade, proliferation marker Ki-67, hormone receptors (ER/PgR) and HER2. HER2 status was also confirmed by FISH. Primary endpoint was the discordance rate (DR) in ER, PgR, HER2 between local and central pathology.

Results. 112 specimens from 10 cancer centers were reviewed. Ten locally ER positive (≥1% ER and PgR) tumours were found HR negative at the central review (DR 12.3%). Ten ER negative tumours at the local evaluation changed in ER positive after central review (DR 32.3%). The overall DR for ER was 17.8% (95% CI, 10.7%-24.8%). Ten PgR positive tumours became PgR negative and 5 PgR negative tumours resulted PgR positive at central review (DR 14.3% and 12.2% respectively; overall DR 13.6% (95% CI, 7.2%-19.9%). Regarding HER2 status, 20 positive samples resulted negative (DR 54%), while 9 HER2 negative were positive at central evaluation (DR: 13.3%) with an overall DR of 26.6% (95% CI, 18.1%-35%). These findings resulted in therapy change in 64 (57%) patients, mainly with avoidance of chemotherapy and trastuzumab prescription. Moreover, changes in percentage of ER and/or PgR from <50% to >50% immunoreactive cells or vice versa were found in 23 tumours and resulted in different treatment choice (exclusive endocrine therapy in most cases).

Conclusion. In our retrospective analysis, the central pathologic review has a significant impact in the decision-making process in early breast cancers, as previously shown in clinical trials.

Further studies are warranted to confirm these provocative results.

A4* RETREATMENT WITH TRASTUZUMAB-BASED THERAPY AFTER DISEASE PROGRESSION FOLLOWING LAPATINIB IN HER2-POSITIVE METASTATIC BREAST CANCER

Gori S.[1], Montemurro F.[2], Spazzapan S.[3], Metro G.[1], Foglietta J.[1], Bisagni G.[4], Ferzi A.[5], Silva R.R.[6], Gamucci T.[7], Clavarezza M.[8], Stocchi L.[1], Fabi A.[9], Cognetti F.[9], Torrisi E.[3], Crivellari D.[3]

[1]Medical Oncology, S. Maria della Misericordia Hospital, Perugia; [2]Unit of Medical Oncology, Institute for Cancer Research and Treatment, Candiolo (TO), [3]Medical Oncology, National Cancer Institute, Aviano; [4]Division of Oncology, Arcispedale S. Maria Nuova, Reggio Emilia; [5]Medicina II-Oncologia Medica, Ospedale Civile di Legnano; [6]Medical Oncology, E. Profili Hospital, Fabriano; [7]Medical Oncology Unit, ASL Frosinone; [8]Medical Oncology, Don Calabria Hospital, Negrar (VR); [9]Regina Elena National Cancer Institute, Rome

Background. Preclinical data suggests that treatment with lapatinib reinduces sensitivity to trastuzumab in HER2+ breast cancer cells.

Patients and methods. Between January 2007 and November 2010, 179 HER2+ MBC were treated with lapatinib and capecitabine at 9 Italian institutions. We evaluated the clinical outcome of 69 patients (38.5%) retreated with trastuzumab after lapatinib progression.

Results. Visceral metastases were identified in 51 (74%) and brain metastases in 16 patients (23%). All patients were pretreated with both trastuzumab and lapatinib-based therapy. We observed with retreatment with trastuzumab-based therapy: 1 CR (2%), 18 PRs (29%) and 10 SD ≥6 months (14%) and 47% of clinical benefit (CB). Median duration of response was 8.1 months (95% C.I. 5.5-10.7). No unexpected toxicities occurred during rechallenge with trastuzumab; most toxicities observed were grade 1-2. Only one patient (1.4%) developed grade 3 cardiotoxicity.

At a median follow-up of 13 months, median PFS was 4.9 months (95% CI 4.2-5.6) and OS 19.4 months (95% CI 14.0-25.0). Median OS was longer for patients experiencing CB (not reached vs 13.4 months for pts without CB, p = 0.002). Brain involvement was associated with lower median OS (17.3 months vs 23.3 months for patients without brain disease; p = 0.021). At multivariate analysis, the risk of death was significantly higher in patients with visceral involvement and in those with CNS involvement with or without other metastatic sites, while it was significantly reduced in patients achieving clinical benefit to rechallenge with trastuzumab-based therapy.

Conclusions. These results show encouraging clinical outcome in HER2+ MBC patients by resuming trastuzumab after disease progression on lapatinib plus capecitabine, with a clinical benefit in 47% of patients progressing during lapatinib-based therapy and overall survival of 19.4 months.

Few clinical data regarding benefit by rechallenge trastuzumab in metastatic breast cancer that progressed during prior lapatinib therapy are available, but these results confirm that HER2 remains an effective therapeutic target even in the presence of disease progression to anti-HER2 treatment.

A5* EARLY BREAST CANCER WITH MODERATE EXPRESSION OF HER2 (IHC 2+) AND NO GENE AMPLIFICATION: A PROGNOSTICALLY DISTINCT SUBGROUP?

Rossi V.[1], Sarotto I.[2], Ponzone R.[3], Maggiorotto F.[3], Tomasi Cont N.[3], Valabrega G.[1], Redana S.[1], Aglietta M.[1], Montemurro F.[1]

[1]Division of Medical Oncology, [2]Division of Surgical Pathology, [3]Division of Gynecological Oncology, Institute for Cancer Research and Treatment (IRCC), Candiolo, Italy

Purpose. Human epidermal growth factor receptor 2 (HER2) positivity in breast cancer (BC) is defined as either strong immunohistochemical (IHC) staining (3+) or moderate IHC staining (2+) with fluorescence-*in situ* hybridization (FISH) proven *HER2* gene amplification. By using these criteria, HER2-positivity has been established as an adverse prognostic factor and a predictive marker of response to anti-HER2 treatment. Tumours with moderate HER2 staining (2+ and no amplification) are grouped with tumours with weak (1+) or no (0+) staining and defined as HER2-negative. We compared the clinical outcomes of women with early BC (EBC) according to HER2 status.

Methods. A total of 772 women undergoing surgery for EBC were retrospectively reviewed. All patients had undergone HER2 testing by the HercepTest and, when needed, by FISH at the same laboratory. The impact of HER2 status on disease-free survival (DFS) was corrected for other clinical and pathological potential covariates by Cox Proportional Regression Analysis**.**

Results. HER2 0+, 1+ 2+ and positive (3+ or FISH+) EBC was found in 261 (33%), 285 (37%), 105 (14%) and 121 (16%) of the patients, respectively. Fifty-five patients with HER2-positive EBC received adjuvant trastuzumab. A total of 192 (25%) DFS events occurred at median follow-up of 29 months (4-55 months). By using HER2 0+ status as reference, multivariate analysis revealed that HER2 2+ status was associated with a significant increase in the risk of a DFS event (HR 2.13, 95% CI 1.33-3.40, p <0.002). HER2 1+ and HER2-positivity in the presence of trastuzumab had no increased DFS risk. HER2-positive patients not receiving trastuzumab had the highest risk of a DFS event (HR 4.58, 95% CI 3.08-6.82, p <0.000).

Conclusion. Moderate HER2 staining (IHC 2+) identifies a group of EBC patients at increased risk of a DFS event. Due to suggestions from large randomized trials that the benefits of trastuzumab may not be limited to HER2-positive tumours, patients with HER2 2+ EBC are ideal candidates for studies testing this hypothesis.

A6* QUALITY INDICATORS FOR BREAST CARCINOMA DIAGNOSTIC AND THERAPEUTIC CARE PATHWAYS (DTCP) IN LOMBARDY. THE INDEX PROJECT

Isa L.[1], Barni S.[2], Agnello M.[3], Giordano M.[4], Tabiadon D.[1], Locatelli W.[5], Azzi M.[6], Mariani S.[7]

Oncology Department: [1]Melegnano MI, [2]Treviglio BG, [4]Como; [3]Sanitary Direction Sacco Hospital, Milan; [5]General Manager ASL Città Milano; [6]General Manager ASL Bergamo; [7]General Manager AO Cremona

Aims and background. This study aims to highlight the areas of the breast cancer DTCP liable to possible improvement actions in order to ensure a more efficient use of resources according to the pathway defined by the guidelines of the Lombard oncological network (ROL). The sections of CIPOMO and the Federation of General Managers of Local Health Companies (FIASO), Lombardy, supported the need to investigate this area of care. The INDEX project presents itself as a means to achieve this common goal.

Patients and methods. The breast cancer DTP has been subdivided into the 4 focus areas, anticipated diagnostics (screening), clinical diagnostics, primitive tumour treatment and follow-up (FU) and it has been evaluated in 10 ASL in Lombardy chosen amongst highly urbanized, mixed urban-rural and mainly rural areas. Data were taken from the Patients Database (Banca Dati Assistiti-BDA). The analysis of the target population was carried out on 368,416 women of age 50-69 in the year 2008. Between January and June 2008, 5,056 women older than 18 have undergone any form of surgery related to breast cancer and a portion of these has been subjected to chemotherapy and/or radiotherapy. It has been possible to trace FU for 2,390 women during July-December 2007.

Results. Screening: gross participation rate varying between 77% and 47%. Average waiting time for further diagnosis in the case of positive result: 18.5 days. Average recall rate for further diagnosis ranging between 8% and 3% for the various ASL. Among the 5,056 women positive to the screening and subsequently surgically treated, 12% of them chose to be treated in a facility different from the one where the mammography was performed; this trend was though extremely variable between the 10 considered ASL (0% to 90%). The average of interval cancers was 0.13%. In one mountain-rural area a more pronounced evidence of breast cancer was observed in the 35-39 age band in relation to the same age band in other areas (9.72% versus 2.9%, respectively). In the case of breast cancer for the general population, therefore not only in relation to this screening, the average waiting time between biopsy and surgery varied between 50 and 20 days. Delayed breast reconstruction took place only for a minor percentage of the total cases (0.36%). 713 women were selected to be treated by chemotherapy; the average waiting time from surgery was of 84 days, with significant variations for two ASL (about 100 days) in relation to the remaining 8 which showed homogenous times below 50 days. 825 women were selected for radiotherapy. In this case the average waiting time from surgery was 111 days with a more homogeneous distribution between the various facilities compared to the chemotherapy. 2390 women were evaluated for the FU. Requested examinations were: yearly mammography in 75% of the cases, abdomen echography in 66% of the cases and bone scan in 19.75% of the cases. Tumour markers CEA and CA-15.3 were performed at least twice during the first follow-up year.

Conclusions. This study highlighted the existence of a large variability in the breast cancer DTCP, especially in relation to treatment, with significant variations from the guidelines. Such variations can have consequences on the treatment efficacy as well as on the effective use of resources. The data flows attainable from BDA represent a precious source of information upon which building a care practice coherent with the guidelines becomes possible. At the same time the usage of BDA data allows for the individuation and completion of improvements stemming from the fruitful interaction between pathology specialists and responsible for system management.

A7 ASSOCIATION OF ABCB1 GENE POLYMORPHISMS WITH ACTIVITY OF TAXANE-BASED THERAPY IN BREAST CANCER PATIENTS

Spaggiari F.[1], Rizzo R.[3], Indelli M.[1], Baricordi O.R.[2], Rimessi P.[2], Ferlini A.[2], Frassoldati A.[1]

[1]Unità Operativa Oncologia Clinica, Azienda Ospedaliera-Universitaria Arcispedale S. Anna, Ferrara; [2]Dipartimento di Medicina Sperimentale e Diagnostica, Sezione di Genetica Medica, Università di Ferrara, Ferrara; [3]Dipartimento di Medicina Sperimentale e Diagnostica, Sezione di Microbiologia, Università di Ferrara, Ferrara

Background. Taxanes are among the most effective agents for breast cancer treatment with significant inter-individual variability in pharmacokinetics which may contribute to the variability of both antitumour activity and toxicity. Genes involved in taxane transport (ABCB1), metabolism (CYP2C8) and activity (CYP1B1) may play a role in efficacy and toxicity.

Aim. To explore the association among known single nucleotide polymorphisms (SNPs) in these three genes and the taxane-induced response in breast cancer patients.

Material and methods. Our retrospective analysis was conducted on 35 selected patients (pts) with locally advanced (7 pts) or metastatic (28 pts) breast cancer treated with taxane-based chemotherapy (paclitaxel or docetaxel at standard dosages). We genotyped our pts for SNPs in the CYP2C8 (alleles *1, *2, *3 and *4), CYP1B1 (alleles *1 and *3) and ABCB1 (1236 C >T; 2677 G >T/A; 3435 C >T) genes by real-time PCR assay.

Results. The taxane-based treatment achieved a complete response (CR) in 2 pts (6%), a partial response (PR) in 17 pts (48%), and a stable disease (SD) in 9 pts (26%). Seven pts showed a disease progression (20%). We observed a significant association between the clinical benefit (CR+PR+SD) with taxane and ABCB1 3435 C >T ($\chi^2 = 4.08$; $p = 0.0433$) and ABCB1 1236 C >T ($\chi^2 = 5.88$; $p = 0.0153$). ABCB1 2677 G >T/A showed a not statistically significant correlation with taxane activity ($\chi^2 = 3.163$; $p = 0.0753$), while no associations were found with CYP2C8 and CYP1B1 alleles. Furthermore we found a significant association with taxane activity when all ABCB1 polymorphisms (1236 C >T, 3435 C >T, 2677 G >T/A) were evaluated together as a haplotype (Fisher's Test, $p = 0.05$).

Conclusions. Our results suggest a role for ABCB1 genotypes in taxane activity. They are supported by some literature data reporting that these ABCB1 SNPs may influence P-glycoprotein expression and transport function. Our results, if confirmed in a larger cohort of patients, might suggest ABCB1 SNPs as predictive biomarkers for taxane activity in breast cancer patients.

A8 UNFAVOURABLE PROGNOSIS IN PT1B HER2 POSITIVE AND TRIPLE NEGATIVE BREAST CANCER PATIENTS

Vaccaro A.[1], Ciancola F.[2], Vici P.[3], Sperduti I.[4], Moscetti L.[5], Pizzuti L.[6], Di Seri M.[2], Ruggeri E.M.[5], Giampaolo M.A.[1], Longo F.[2], Gamucci T.[1]

[1]ASL Frosinone, Medical Oncology Unit, Frosinone, Italy; [2]University La Sapienza, Medical Oncology Unit, Rome, Italy; [3]Regina Elena National Cancer Institute, Medical Oncology Unit, Rome, Italy; [4]Regina Elena National Cancer Institute, Bio-Statistics Unit, Rome, Italy; [5]Belcolle Hospital, Medical Oncology Unit, Viterbo, Italy

Background. Controversy still exists about adjuvant treatment decision for small node negative (N0) early breast cancer (BC). The objective of our analysis is to evaluate recurrence risk in patients (pts) with pT1abc, N0 BC accordingly with some prognostic biological factors.

Methods. We retrospectively evaluated 900 pts from 4 Italian centers who underwent surgery between 2000 and 2010. For survival analysis we evaluate only pts enrolled until December 2008 (773 pts) to obtain a minimum follow-up (FU) of 3 years (yr).

Results. Median age 58 (range 21-86); premenopausal 28%; invasive ductal carcinoma 87%; Ki 67 >15% 28%; histologic grade G1 20%, G2 50%, G3 19%, no data in 11%; pT1a 8%; pT1b 38%; pT1c 54%. We defined 3 cohorts: ER+ 75%; HER2 overexpressed or amplified (HER2+) 14%; triple negative (TN) 11%. All ER+ pts received adjuvant hormonal treatment while 33% of pts (pT1c 70%, pT1b 27%, pT1a 3%) chemotherapy (CT). In HER2+ CT (plus trastuzumab in 54%) was administered in 57/97 pts (59%) and in TN pts 51/74 (69%). Median FU was 67 months. To date 14% of pts recurred. The 5-yr disease free survival (DFS) and overall survival (OS) were 89.8.% and 98.0%. DFS according to different cohorts is shown in the Table. In pT1bc pts there is a higher rate of recurrence (HR 1.73, 95% CI 1.06-2.83; $p = 0.03$) in HER2+ and TN and DFS according to tumour size is b+c vs a with HR 2.20 (95% CI 0.70-6.93; $p = 0.18$). At the Cox univariate analysis Ki67 and grading are significant factors. At the multivariate analysis histological grade is confirmed as independent factor (HR 2.10, 95% CI 1.28-3.45, $p = 0.003$).

Conclusions. pT1b or c, N0, HER2+ and TN BC have a significant high risk of recurrence. The better prognosis of pT1c HER2+ and TN pts is presumably related to the high percentage of pts treated with adjuvant therapy. Effective therapy should be considered for all these unfavorable prognostic subgroups.

DFS			5-yr %	p
All	pT1	a	96.3	0.35
		b	89.2	
		c	89.4	
ER+	pT1	a	100	0.12
		b	93.6	
		c	89.8	
TN	pT1	a	100	0.65
		b	76.8	

A9 CLINICAL IMPLICATIONS OF PROGESTERONE RECEPTOR STATUS IN LOCOREGIONAL RECURRENCE OF ESTROGEN RECEPTOR POSITIVE BREAST CANCER PATIENTS

Bogina G.[1], Lunardi G.[1], Coati F.[1], Marconi M.[1], Federico M.[2], Cortesi L.[2], Cirilli C.[2], Ficorella C.[3], Cannita K.[3], Irelli A.[3], Venturini M.[1]

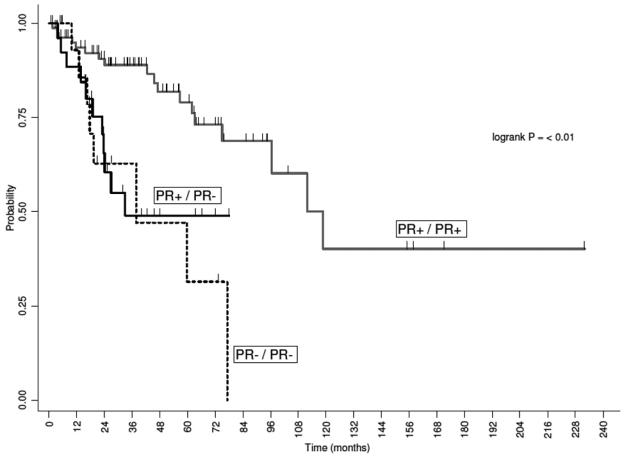
[1]Ospedale S. Cuore Don Calabria-Negrar (VR); [2]Università di Modena e Reggio Emilia; [3]Università degli Studi de L'Aquila

Background. Locoregional recurrences (LR) may occur in patients after primary breast cancer. A high loss rate of progesterone

receptor (PR) status in LR has been previously reported. On this way, we examined whether this finding could have any clinical impact in estrogen receptor (ER) positive patients. Aim of this study was to evaluate the distant metastasis-free survival (DMFS) after LR in patients with ER positive primary tumours (PT), according to change in expression of PR status between PT and corresponding LR.

Methods. We collected pathological features and outcome in breast cancer patients who experienced LR. Data were from three Italian oncology centers. According to the ASCO/CAP guidelines we defined as positive the tumours with ER/PR ≥1%; we considered as shifted those cases that changed from ≥1% to <1%. DMFS was defined as elapsed months since LR to a distant metastasis (DM). Patients with DM prior or synchronous to LR were excluded.

Results. Data from 134 patients were analysed. Figure reported DMFS after LR according to PR status. Ninety patients had PR positive PT and LR (PR+/PR+), 18 patients had PR negative PT and LR (PR-/PR-) and 26 patients, with PR positive PT, had lost PR in LR (PR+/PR-). Median DMFS was 119 months, 38 months and 32 months in PR+/PR+, PR-/PR- and PR+/PR- patients, respectively (logrank test p value <0.01).



Conclusions. Loss of PR in LR determined a lower time DM subsequent to the first LR. In patients with ER positive LR, PR lost in LR may correlate with a more aggressive behaviour of tumour. Endocrine therapy may not be enough for these patients who could benefit from a more aggressive therapeutic approach.

A10 INCIDENCE OF HEPATITIS B AND C INFECTIONS IN EARLY BREAST CANCER PATIENTS AND IMPACT ON SYSTEMIC TREATMENT

Levaggi A., Iacono G., Giraudi S., Bighin C., De Maria A., Lambertini M., Canavese G., Pronzato P., Del Mastro L.

National Institute for Cancer Research, Genoa

Background. Little information exists about the incidence of hepatitis B and C infections in early breast cancer patients and the impact on systemic treatment.

Methods. We retrospectively reviewed hepatitis B or C serology of 746 consecutive patients with early breast cancer treated at National Institute for Cancer Research between January 2009 and March 2011. All patients were screened for hepatitis Bs antigen (HBsAg), HBc antibodies (HBcAb), HBs antibodies (HBsAb) and HC (HCV) antibodies. Patients with positive serology were elegible for this study. Data collected included patients and tumour characteristics, treatment received, changes in aminotransferases and impact on systemic treatment.

Results. 170 patients were excluded because serology was not available. Among 576 evaluable patients we indentified 28 (4.8%) patients vaccinated against HBV and 69 (12%) with positive serology: 17 patients (2.9%) with HCV infection, 7 (1.2%) with occult HBV (HBsAg negative, HBsAg Ab negative, HBcAg Ab positive), 40 (6.9%) with cleared HBV (HBsAg negative, HBsAg Ab positive, HBcAg Ab positive) and 6 (1%) with chronic HBV (HBsAg positive, HBsAg Ab negative, HBcAg Ab positive). Eleven patients (16%) experienced a grade 1 or greater elevation in aminotransferases during systemic therapy as follows: CTC grade 1 (five patients), grade 2 (eight) and grade 3 (one) (Table 1). Among the patients who developed an elevation in aminotransferases, 6 (54.5%) had HCV infection, 2 (18%) had chronic HBV while no patients had occult HBV. Among patients with transaminitis two patients HCV positive (18%) required discontinuation of systemic therapy: one patient discontinued hormonetherapy and one trastuzumab.

Table 1

	CT ± OT	CT + T ± OT	OT	Total
HCV (17 pts)	1 (5.8%)	1 (5.8%)	4 (23.5%)	6 (35.1%)
Occult HBV (7 pts)	0	0	0	-
Cleared HBV (40 pts)	1 (2.5%)	2 (5%)	0	3 (7.5%)
Chronic HBV (6 pts)	2 (33.3%)	0	0	2 (33.3%)

CT = chemotherapy; OT = hormonetherapy; T = trastuzumab.

Conclusion. About 12% of newly diagnosed breast cancer patients have positive serology for viral hepatitis and within this group about 16% may develop transaminitis during systemic treatment. Discontinuation of systemic treatment can occur in about 18% of patients with elevation in transaminases. Pretreatment serum detection of viral hepatitis B and C antigen and antibodies is useful for adeguate monitoring of liver function during anti-neoplastic therapy.

A11 CLINICAL OUTCOME OF LOCALLY ADVANCED (LABC) OR METASTATIC BREAST CANCER (MBC) PATIENTS WITH TRIPLE-NEGATIVE PHENOTYPE WHO RECEIVED NON-PEGYLATED LIPOSOMAL DOXORUBICIN (MYOCET) PLUS VINORELBINE OR CYCLOFOSPHAMIDE AS FIRST-LINE CHEMOTHERAPY (CT)

Ciccarese M.[1], Colucci G.[2], Giotta F.[2], Bordonaro R.[3], Maiello E.[4], Del Prete S.[5], Gebbia V.[6], Filippelli G.[7], Pisconti S.[8], Cinieri S.[9], Romito S.[10], Riccardi F.[11], Cairo G.[1], Chiuri V.E.[1], Forcignanò R.[1], Petrucelli L.[1], Saracino V.[1], Lorusso V.[1]

[1]Ospedale Vito Fazzi, Lecce, Italy; [2]Istituto Oncologico, Bari, Italy; [3]Catania Hospital, Catania, Italy; [4]Ospedale Casa Sollievo della Sofferenza IRCCS, San Giovanni Rotondo (FG), Italy; [5]Frattamaggiore Hospital, Frattamaggiore (Napoli), Italy; [6]Ospedale La Maddalena, Palermo, Italy; [7]Paola Hospital, Paola (Cosenza), Italy; [8]Taranto Hospital, Taranto, Italy; [9]Ospedale Perrino, Brindisi, Italy; [10]Ospedali Riuniti, Foggia, Italy; [11]Ospedale Cardarelli, Napoli, Italy

Background. Triple-negative (TN) breast cancers are defined as a lack of expression of ER, PgR and HER2. We retrospectively analyzed the clinical outcome in patients with LABC or MBC cancer who received non-pegylated liposomal doxorubicin (Myocet) with cyclophosphamide or vinorelbine as first-line treatment, focused on TN phenotype.

Methods. A multicenter randomized phase II study was planned to enroll 250 patients (pts) with advanced breast cancer refractory to endocrine treatment. Eligible pts must have PS (ECOG) ≤2 and measurable disease. Adjuvant or neo-adjuvant chemotherapy with anthracyclines was allowed as well as prior endocrine therapy. Patients assigned to arm A received Myocet 60 mg/m^2 plus cyclophosphamide 600 mg/m^2 1 q21 (MC). Patients in arm B received Myocet 50 mg/m^2 plus vinorelbine 25 mg/m^2 iv on day 1, and 60 mg/m^2 on day 8 po, q21 (MV). The primary endpoint was response rate (RR), whereas safety was one of the secondary endpoints.

Results. Between July 2006 and December 2010, 253 pts were treated; for 39 of these with TN phenotype (arm A pts = 17, arm B pts = 22), activity results are available. Complete plus partial response was observed in 10/17 (59%) pts treated with MC and in 7/22 (32%) pts treated with MV, respectively (p = 0.17). Moreover, 4 pts in arm A and 6 pts in arm B showed disease stabilization (SD), with a clinical benefit of 82% and 59% respectively. Overall, 17/39 (44%) pts achieved a clinical response plus 10/39 (26%) SD, with a disease control rate of 70%. In MC group, 76% of pts received ≥6 cycles of CT at full dose, with a median cyclophosphamide dose intensity 181 mg/m^2/week.

Conclusion. Our data suggest a superior, even if not significant, activity of cyclophosphamide as compared to vinorelbine when combined with doxorubicin, in TN breast cancer. Moreover, cyclophosphamide dose intensity seems to positively relate to RR and doxorubicin related toxicity, in particular cardiotoxicity is negligible with the non-pegilated liposomal formulation.

A12 SHOULD WE ADOPT DIFFERENT KI67 LI CUT-OFFS IN DIFFERENT ER POSITIVE GRADING-BASED EARLY BREAST CANCER (EBC) GROUPS?

Ferro A.[1], Caldara A.[1], Eccher C.[2], Triolo R.[1], Di Pasquale M.C.[1], Aldovini D.[3], Cuorvo L.V.[3], Barbareschi M.[3], Berloffa F.[3], Galligioni E.[1]

[1]Oncologia Medica, Trento; [2]Anatomia Patologica, Trento; [3]Fondazione Bruno Kessler, Trento

Background. The Ki67 labeling index (LI) is a measure of tumour proliferation. The 2009 St Gallen Consensus considered Ki67 as an important parameter for the addition of chemotherapy to endocrine therapy in hormone-receptor-positive EBC, suggesting three cut-offs: low <15%, intermediate 15-30% and high >30%. We evaluated if these cut-offs can be used in different subgroups of EBC, or if to apply different cut-offs in distinct biological setting based on G.

Methods. Ki67 LI 1 was identified by immunohistochemical staining in 3802 EBC pts treated from 1995 to 2008. Median age was 61. The relationship with clinical-pathological parameters and the prognostic significance of KI67 LI was investigated in all EBCs and in subgroups of ER+ cases based on homogeneous grading (656 G1, 1535 G2, 1113 G3).

Results. Median Ki67 LI values were 22% in all cases and 10, 20 and 36% in ER+ G1, G2 and G3 respectively. High Ki67 LI was significantly (p <0.001) associated with younger age, ductal type, greater size, positive N, poor G, absent or low ER/PR, positive HER-2, triple negative subtypes, larger use of chemo ± hormonotherapy. At median follow-up of 51 months DFS and OS were 84 and 85% respectively in high, 89 and 90% in intermediate, 92 and 94% respectively in low Ki67 LI group (p <0.001). There were 456 relapses (12%): 207 (5.4%) in high, 136 (3.6%) in intermediate and 113 (3%) in low Ki67 LI group. Using median Ki67 LI value for different homogenous ER+ grading groups (ER+GG) we stratified these populations in low and high risk:

Subgroups		At median follow-up DFS (%)	p-value	At median follow-up OS (%)	p-value
G1	high	90	0.058	93	0.005
	low	95		97	
G2	high	93	<0.001	94	0.001
	low	87		90	
G3	high	87	NS	85	0.008
	low	88		87	

Conclusions. Ki67 LI confirms to be a significant prognostic biomarker for DFS and OS in EBC, associated with other clinical-pathological characteristics. Cut-offs are different into ER + GG. They can categorize at least two biological entities in every grading group providing additional prognostic information in planning therapies and outcome prediction.

A13 RELATIVE RISK OF RECURRENCE (RR) OVER TIME IN ER POSITIVE AND NEGATIVE T4 BREAST CANCER PATIENTS ACHIEVING LESS THAN pCR (<pCR) AFTER PRIMARY CHEMOTHERAPY: A REVERSAL TREND OF RECURRENCE BEYOND 60 MONTHS AFTER DIAGNOSIS

Ionta M.T.[1], Notari F.[1], Atzori F.[1], Pusceddu V.[1], Valle E.[2], Murru M.[1], Chiappe A.[1], Minerba L.[3], Massidda B.[1]

[1]Department of Medical Oncology, Hospital-University, Cagliari, Italy; [2]Department of Medical Oncology, Oncologic Hospital, Cagliari, Italy; [3]Department of Public Health, University, Cagliari, Italy

Background. It is widely assumed that patients (pts) who achieve pCR have significantly better outcomes compared with patients with <pCR, regardless of hormone receptor status. Emerging data suggest that achieving <pCR identifies a heterogeneous group with different risks of recurrence and death, being ER- the subgroup with the worst prognosis.

Objectives. Aim of our study was to evaluate the relative risk of recurrence (RR) over time in ER-positive and ER-negative <pCR patients.

Methods. We analyzed 139 consecutive <pCR T4 pts, of whom 85 were ER+ (cut-off 10%) and 54 were ER-. Median age was 53 y (range 29-73). Median follow-up was 137 months (range 8-233). All pts received primary anthra-based chemotherapy with or without taxanes followed by endocrine therapy for 5 years, if hormone receptor positive. We examined the RR of recurrence at 0-24, 25-60, 61-120 and beyond 120 months interval after diagnosis.

Results. For all 139 pts, the total number of pts with recurrence was 95 (68%), 54 (63%) in ER+ and 41 (76%) in ER-. For

the entire group and both in ER+ and in ER-, the RR of recurrence was greatest for the interval between 0-24 months, then decreased rapidly in ER- and slowly in ER+ through the 25-120 m interval. For the 0-24 m and 25-60 m intervals the RR of recurrence was higher for ER- pts and after 60 m it crossed and beyond 60 m the RR of recurrence was higher in ER+ than in ER- pts. Notably, beyond 120 months we observed a little second peak, higher in ER+ than in ER- pts. Nine of 10 relapses (7 ER+ and 2 ER-) occurred between 120 to 180 m interval. In the first 24 m ER- pts were 86% more likely to relapse compared with ER+, vice versa between 61-120 and beyond 120 m intervals, ER- pts were 19% and 18% less likely to relapse, respectively, compared with ER+ pts.

Conclusions. The present study confirmed the previous reports which showed unfavorable prognosis of the <pCR patients with negative ER status, due to their higher relative risk of recurrence between 0 to 60 months interval. The ER+ recurrences occurred more frequently in late follow-up. A reversal of recurrence between ER positive and negative patients beyond 60 months after diagnosis was detected. The fact might indicate the importance of long term adjuvant hormone therapy for T4 ER positive breast cancer patients with <pCR after primary chemotherapy.

	No.*	%	0-24 m	RR	25-60 m	RR	61-120 m	RR	>120 m	RR
Global relapses	95/139	68	52/139	1.3	22/136	0.70	11/114	0.50	10/88	1.1
ER+	54/85	63	25/85	1.02	14/83	0.65	8/66	0.49	7/43	0.69
ER-	41/54	76	27/54	1.9	8/53	0.75	3/48	0.40	3/45	0.57

*No. relapses/pts at risk

A14 MAMMAPRINT AND Ki67 IN BREAST CANCER PATIENTS UNDERGOING ADJUVANT HORMONAL THERAPY

Pizzutilo P.*, Indelli M.*, Da Ros L.*, Querzoli P.°, Schirone A.*, Santini A.*, Donati D.*, Frassoldati A.*

**U.O. Oncologia Clinica, °Anatomia Patologica, Azienda Ospedaliero-Universitaria S. Anna, Ferrara*

Background. Mammaprint® can discriminate breast cancer patients with good or bad prognosis, and has been considered a valuable tool in case of intermediate risk classification with the classical clinical and pathological parameters, in order to decide for using chemotherapy.

Methods. Mammaprint® analysis was performed in 120 consecutive patients (age 38-93, mean 65) with invasive operable breast cancer (T1-4N1-3M0) diagnosed from 2008 to December 2009, independently from the treatment choice. This report is aimed to evaluate the concordance between Mammaprint® results and the risk category based on NPI, Adjuvantonline and St. Gallen criteria, and with the Ki67 value (using a 14% cut-off). Moreover, to evaluate the potential clinical impact of this genomic predictor in daily clinical practice, we evaluated the occurrence of early relapse in patients receiving hormonal therapy only, according to the Mammaprint® risk group and to the Ki67 levels.

Results. 103 out of 120 samples were evaluable for Mammaprint®: 42 (40.8%) were classified as low and 61 (59.2%) as high risk. Mammaprint® results were significantly correlated with histological grade ($p < 0.0001$), proliferative activity ($p < 0.0001$), estrogen ($p = 0.002$) and progesterone receptor status ($p = 0.029$) and with HER2 status ($p = 0.030$). If adjusted for clinical-pathologic evaluation systems, the results showed good correlation with the St. Gallen risk classification ($p = 0.004$) and with the NPI ($p = 0.009$), but not with Adjuvantonline results ($p = 0.183$).

Mammaprint® results indicated a good prognosis in 13 out of 44 (29.5%) patients assigned to chemotherapy ± hormones (based on the clinical-pathological tumour characteristics). On the contrary, Mammaprint® indicated a poor risk in 25 out of 52 (48%) patients assigned to hormonal therapy only. In these 52 patients, we evaluated also the relationship between Mammaprint®, KI67 and the occurrence of early recurrence. Twenty-seven patients had Mib-1 <14% and 25 patients ≥14%. Among 27 patients with low Mib-1, 18 were Mammaprint® low and 9 high risk. Among 25 patients with high Mib-1, 9 were Mammaprint® low and 16 high risk. After 2 years median follow-up, we observed 2 relapses, both in patients with Mib-1 high (1 Mammaprint® low and 1 high risk).

Conclusion. These data confirm the unclear utility of Mammaprint® in our clinical practice, and seems to corroborate the clinical value of Ki67 levels in patients otherwise considered at good prognosis.

A15 ANGIOGENESIS-RELATED GENE POLYMORPHISMS AS POTENTIAL PREDICTIVE BIOMARKER FOR BEVACIZUMAB IN METASTATIC BREAST CANCER PATIENTS

Di Salvatore M.[1], Inno A.[1], Isgrò M.A.[2], Nazzicone G.[1], Lo Giudice L.[1], Rodriquenz M.G.[1], Orlandi A.[1], Santonocito C.[2], Capoluongo E.[2], Astone A.[1], Barone C.[1]

[1]Division of Medical Oncology, [2]Division of Biochemistry, Università Cattolica del Sacro Cuore, Roma

Background. The addition of bevacizumab to first-line chemotherapy has slightly improved the outcome of metastatic breast cancer (mBC) patients; however, the identification of predictive biomarkers may help to select patients who may potentially achieve the most benefit from the anti-VEGF drug. We have investigated the role of some angiogenesis regulating genes as potential predictive or prognostic biomarkers.

Methods. Genomic polymorphisms of VEGF-1154 G/A, VEGF-936 C/T, VEGF-2578 C/A, eNOS-786 T/C, eNOS-849 G/T and IL8-251 T/A were assessed in 32 patients treated with bevacizumab plus paclitaxel as first-line treatment for mBC.

Results. Overall response rate (ORR) was 65% and median progression-free survival (mPFS) was 12 months. Main G3-4 adverse events were neutropenia, hypertension, fatigue (6.5%) and neuropathy (6.5%). Noteworthy, 2 patients died during the treatment, one for bowel perforation and the other for febrile neutropenia. No significant association was observed between any investigated polymorphism and ORR or treatment-related toxicity. However, mPFS was significantly shorter for patients with IL8-251 T/T homozygous genotype when compared whit those with A/T or A/A genotypes (10 vs 15 months; HR 2.54, 95% CI 1.2-8.02; $p = .01$). Also patients with eNOS-786 C/C genotype had a mPFS worse than patients with T/C and T/T genotypes (11 vs 14 months, HR 2.39, 95% CI 1.01-13.03, $p = .04$).

Conclusions. Our data suggest that IL8-251 T/T and eNOS-786 C/C homozygous genotypes may negatively affect the outcome of mBC patients treated first-line bevacizumab plus paclitaxel. This interesting finding deserves larger prospective evaluation to be confirmed as predictive biomarkers of bevacizumab efficacy.

A16 WHOLE MICRORNA PROFILING OF BRCA1-DEFECTIVE HCC1937 BREAST CANCER CELLS SUGGESTS A ROLE OF MIR-34A IN THE MECHANISMS UNDERLYING THE ENHANCED PLATINUM SENSITIVITY

Di Martino M.T.[1], Ventura M.[1], Leone E.[1], Guzzi P.H.[2], Cannataro M.[2], Foresta U.[1], Pitari M.R.[1], Gallo Cantafio M.E.[1], Tomaino V.[1], Gullà A.[1], Rota R.[3], Tassone P.[1], Tagliaferri P.[1]

[1]Medical Oncology Unit and T. Campanella Cancer Center, [2]Bioinformatics Laboratory, Department of Experimental and Clinical Medicine, Magna Græcia University Campus Salvatore Venuta, Catanzaro, Italy; [3]Laboratory of Angiogenesis, Department of Oncohematology, Ospedale Pediatrico Bambino Gesù, IRCCS, Roma, Italy

BRCA1 plays a critical role in DNA-damage repair mechanisms elicited by cell exposure to anti-tumour agents. HCC1937 is a BRCA1-defective breast cancer cell line which discloses higher sensitivity to cisplatinum (CDDP) as compared to the derivative HCC1937/wtBRCA1 cell line which has been reconstituted by normal BRCA1 full-length cDNA transfection (Tassone et al. 2003, Br J Cancer). We previously found a differential modulation of Notch signaling after CDDP exposure in HCC1937 cell line as compared to a reconstituted clone, with a strong down-regulation of Notch 1, 2 and 3 expression at mRNA and protein level together with other genes involved in the Notch signalling network (Di Martino et al. 2008, SABCS #5062). Moreover, we showed that the combination of the pan-Notch inhibitor, gamma-secretase inhibitor XII (GSI-XII), with CDDP produced a significant synergistic cytotoxic effect in BRCA1-defective cells (Ventura et al. 2009, SABCS #3128). On these bases, we have explored the whole microRNA (miRNA, miR) microarray profile of the HCC1937 and HCC1937/wtBRCA1 cell lines by GeneChip miRNA Array (Affymetrix, Santa Clara, CA), the most comprehensive miRNA platform, in the aim to identify miRNAs whose expression might correlate to the cisplatinum sensitivity of the BRCA1-defective tumours. We identified 22 miRNAs and 3 small nucleolar RNAs (snoRNAs) differently expressed in HCC1937 versus HCC1937/wtBRCA1 breast cancer cells. Among them, miR-34a shows higher expression levels in HCC1937 versus HCC1937/wtBRCA1. This finding appears of specific interest because Notch is a validated direct target of miR-34a whose ectopic expression induces cell-cycle arrest, apoptosis and senescence in cancer cells. Interestingly, it has been recently reported the miR-34 family is indeed modulated by cisplatinum treatment. On these findings we may speculate that CDDP sensitivity is directly correlated to higher miR-34a expression through the inhibition of Notch pathway. These findings warrant investigation of miR-34a and Notch signaling activation levels as predictive markers of CDDP sensitivity.

Supported by MIUR.

A17 FIRST-LINE BEVACIZUMAB (B) PLUS PACLITAXEL (P) IN HER2-NEGATIVE (HER2-ve) METASTATIC BREAST CANCER (mBC): EFFICACY AND SAFETY IN AN ITALIAN MULTICENTER RETROSPECTIVE STUDY

Andreis D.[1], Scandurra G.[2], Santini D.[3], Gucciardino C.[3], La Verde N.M.[4], Girelli S.[4], Alabiso I.[5], Saetta A.[6], Atzori F.[7], Collovà E.[8], Ferzi A.[8], Gori S.[9], Lipari H.[10], Ibrahim T.[11], Saggia C.[12], Marcon I.[13], Generali D.[1]

[1]U.O. Multidisciplinare di Patologia Mammaria, A.O. Istituti Ospitalieri di Cremona; [2]Day Hospital, Humanitas Centro Catanese di Oncologia; [3]Dipartimento di Medicina Oncologica, Università Campus Bio-Medico di Roma; [4]U.O. di Oncologia Medica, A.O. Fatebenefratelli e Oftalmico, Milano; [5]S.C. Oncologia Medica, Ospedale Civile di Ivrea; [6]U.O. di Oncologia, Fondazione Istituto San Raffaele D. Giglio di Cefalù; [7]Struttura Complessa di Oncologia Medica, A.O.U. di Cagliari; [8]II Oncologia Medica, Ospedale Civile di Legnano; [9]Oncologia Medica, A.O. di Perugia; [10]U.O. di Oncologia Medica, A.O. Ospedale Cannizzaro, Catania; [11]Centro di Osteoncologia, IRST, Meldola; [12]S.C.D.U. di Oncologia, A.O.U. Ospedale Maggiore della Carità, Novara; [13]U.O. di Oncologia, A.O. Ospedale di Circolo e Fondazione Macchi, Varese

Background. The combination of B with P as first-line treatment for patients (pts) with HER2-ve mBC showed clinical benefits in terms of progression-free survival (PFS) and objective response rate (ORR) without an effect on overall survival (OS). This Italian multicenter retrospective study wanted to evaluate the first-line B plus P in term of efficacy and safety in routine oncology practice.

Methods. A total of 112 female pts with HER2-ve mBC, ECOG performance status 0-1, received B 10 mg/kg every 2 weeks or 15 mg/kg every 3 weeks combined with P. PFS and OS were estimated using the Kaplan-Meier method and compared with log-rank test. Chi-square test was employed for comparison of proportion.

Results. Patients characteristics included: median age 56.9 years; ≥3 sites of lesion 13.4%; previous (neo)adjuvant chemotherapy (CT) 70.5% (taxane-based CT 24.1%).

After a median follow-up of 9.5 months, 61 pts progressed and 26 died. Fifty-six pts (52.8% of evaluable pts) attained a disease response: 16 complete responses and 40 partial responses. Median PFS and OS were 9.2 and 24.4 months, respectively. ≥3 sites of lesion were associated with a significant worse PFS ($p = 0.001$). No associations were found with clinical endpoints based on biological variables (ER, Ki-67) stratification. Previous treatment in neo(adjuvant) setting with taxane-based regimens had a significant less chance to obtain disease response ($p < 0.001$), and worse PFS ($p = 0.008$) and OS ($p < 0.001$).

The majority of adverse events (AEs) were mild or moderate. Grade ≥3 AEs included hypertension (3.6%), neutropenia (1.8%), anemia (0.9%), thromboembolic events (0.9%), gastrointestinal perforation (0.9%) and stomatitis (0.9%). The occurrence of hypertension (all grades, 20.5%) was significantly associated with better ORR (81.8% vs 45.2%; $p = 0.002$) and with a trend (not significant) of better PFS ($p = 0.076$).

Conclusions. The efficacy and safety data of B plus P collected in this study were consistent with results from first-line trials. Pre-treatment with taxane was associated with a worse prognosis. We also confirmed hypertension as significant predictor of B activity.

A18 TRASTUZUMAB-BASED COMBINATIONS FOR HER2-POSITIVE METASTATIC BREAST CANCER (MBC): WHICH OPTIMAL CHEMOTHERAPY PARTNER? RESULTS OF A SINGLE CENTER RETROSPECTIVE STUDY

Bernardo G.[1], Palumbo R.[1], Riccardi A.[2], Bernardo A.[1], Poggi G.[1], Teragni C.[1], Sottotetti F.[1], Tagliaferri B.[1], Strada M.R.[3]

[1]Operative Unit of Medical Oncology II, [2]Department of Medical Oncology, University of Pavia; [3]Operative Unit of Rehabilitative Oncology, Fondazione Salvatore Maugeri-RCCS, Pavia

Background. The activity of trastuzumab-based chemotherapy (CT) in HER2-positive MBC is now well-established, but the question of the optimal antineoplastic partner remains a relevant issue. We performed a retrospective comparison of the clinical outcomes associated with different trastuzumab-CT combinations.

Patients and methods. Patients for this analysis were selected from a monoinstitutional database containing the data of women with HER2-positive MBC (IHC3+ or FISH positive) receiving first-line trastuzumab-based CT between February 2005 and December 2008. Treatment activity was assessed according to the WHO criteria, time to progression (TTP) and overall survival (OS) were calculated by the Kaplan Meier method (intent-to-treat analysis).

Results. A total of 147 women with measurable disease were evaluated: 57 received trastuzumab with weekly vinorelbine (25 mg/m^2 until tumour progression), 48 trastuzumab plus docetaxel (75-100 mg/m^2 every 3 weeks for 6-8 cycles), 42 a triple combination of three-weekly trastuzumab plus oral vinorelbine (60 mg/m^2 days 1 and 8 q 21) and capecitabine (1000 mg/m^2 bid days 1->14, every 3 weeks). ORR was 76% in trastuzumab + vinorelbine group, 68% in the docetaxel-based regimen and 72% in the triple combination. There was no significant difference in median TTP according to treatment type (14, 11 and 12 months, respectively, p = 0.62); median OS was 36 months, 32 and 34 months, respectively (p = 0.48). More treatment related grade 3-4 toxicities were recorded in the docetaxel-treated population. Following progression, 98 women continued trastuzumab-based CT as second or subsequent lines of treatment; with a median gain in OS of 12 months compared to women receiving only CT (p <0.05). In multivariate analysis the number of trastuzumab-based regimens was significantly correlated to OS (p = 0.02), while no correlation was found between the survival benefit and the different type of CT.

Conclusions. Our results show that all the 3 trastuzumab-based combinations were highly active as first-line treatment of HER2-positive MBC, without significant differences in clinical outcomes, also confirming that benefit of continuing trastuzumab beyond progression was independent from the CT partner.

A19 ADJUVANT TRASTUZUMAB IN HER2-POSITIVE EARLY BREAST CANCER WOMEN OLDER THAN 60 YEARS: DATA FROM "REAL WORLD"

Fini F.[1], Cioffi G.[2], Pulignano G.[1], Boccardi L.[1], Lombari C.[3], Carluccio E.[4], Severini D.[5], Frattini S.[6], Pennacchietti L.[7], Tuccia F.[8], Basurto C.[9], Gori S.[9]

[1]Cardiologia I, A.O. San Camillo, Roma; [2]U.O. Cardiologia, Casa di Cura Villa Bianca, Trento; [3]S.C. Cardiologia, Istituto Pascale, Napoli; [4]U.O. Cardiologia e Fisiopatologia Cardiovascolare, A.O. Perugia; [5]U.O. Cardiologia, Città di Castello; [6]Cardiologia, Spedali civili, Brescia; [7]U.O. Cardiologia, Ospedale Murri, Fermo, [8]U.O. Oncologia, Belluno, [9]Oncologia Medica, Azienda Ospedaliera di Perugia

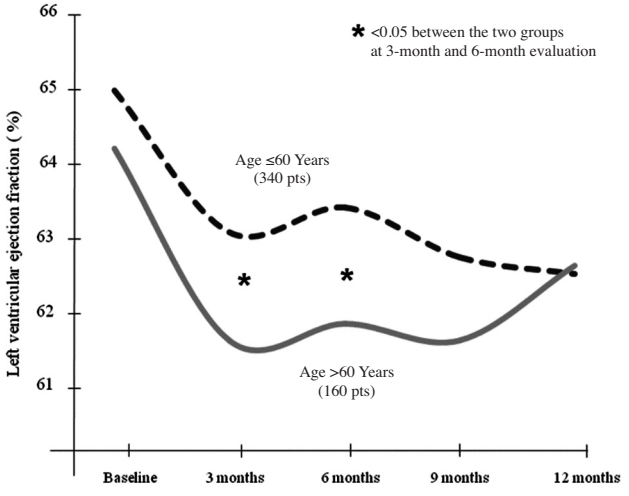
Background. Adjuvant trastuzumab improved DSF and OS in HER2 + EBC patients, but older patients are under-represented in randomized clinical trials.

Patients and methods. Between January 2008 and June 2009, 499 consecutive HER2+EBC patients were treated with adjuvant trastuzumab at 10 Italian institutions.

Cardiotoxicity was defined according to CTCAE–NCI-2.0. LVEF was evaluated by echocardiography at baseline and at 3-6-9-12 months during trastuzumab-therapy.

We evaluated prevalence and clinical characteristics of women older than 60 years; feasibility of adjuvant trastuzumab in this setting of patients; prevalence and predictors of trastuzumab- cardiotoxicity. At 12-month evaluation, any occurrence of symptoms of heart failure and/or decrease greater than 10 points% of LVEF were recorded.

Results. 160 of 499 patients had >60years (32%). They presented more frequently hypertension (48 vs 16%), diabetes (11 vs 3%), renal dysfunction (17 vs 6%) and dyslipidemia (26 vs 10%) and received more frequently ACEi (40 vs 8%) and beta-blockers (20 vs 8%) than the younger patients. Type and dose of chemotherapic agents were similar between the two groups as the LVEF at baseline (65 ± 7 vs 65 ± 6%, p = ns) and at 12-month evaluation (63 ± 6 vs 63 ± 6%, p = ns). However the clinical course during the time of chemotherapy was very different (see Figure):



Symptoms of CHF and/or LVEF reduction >10 points% were detected in 6% and 33% of patients >60years (p <0.05) and 2% and 23% of <60years, respectively (p <0.05). Trastuzumab was discontinued in 10% of older and 4% of younger patients (p = 0.003); the total number of cycles of trastuzumab administered was 16.0 and 17.3, respectively (p = 0.02). Trastuzumab was restarted in 44% of patients >60years and in 58% of ≤60 years (p = ns).

Conclusion. In clinical practice, 32% of HER2+EBC patients treated with adjuvant trastuzumab are older than 60 years and are at increased cardiovascular risk. Although these patients receive more frequently drugs for controlling cardiovascular risk factors, they experience more frequently clinical events and episodes of trastuzumab induced cardiotoxicity than patients who are ≤60 years.

A20 RENAL FUNCTION ON DEVELOPMENT OF CARDIOTOXICITY ASSOCIATED WITH TRASTUZUMAB ADJUVANT THERAPY FOR HER2-POSITIVE (HER2+) EARLY BREAST CANCER (EBC)

Russo G.[1], Laveder F.[2], Latorre A.[3], Bovelli D.[4], Pacilio C.[5], Giustini L.[6], Gabrielli D.[7], Generali D.[8], Di Tano G.[9], Boccardi L.[10], Pulignano G.[10], Stocchi L.[11], Foglietta J.[11], Gori S.[11]

[1]A.S.S. n.1 Centro Cardiovascolare, Trieste; [2]Unità Operativa di Oncologia, Ospedale San Martino ASL1 Veneto, Belluno; [3]U.O. di Oncologia Medica e Sperimentale IRCCS, Istituto Tumori "Giovanni Paolo II", Bari; [4]U.O. Cardiologia, A.O. Terni; [5]Struttura Complessa di Oncologia Medica Senologica, Istituto Pascale, Napoli; [6]U.O. Oncologia, Ospedale A Murri, ZTL11 Fermo; [7]U.O. Cardiologia-Utic, Ospedale A. Murri, ZTL11 Fermo; [8]U.O. Oncologia, Azienda Istituti Ospitalieri, Cremona; [9]U.O. Cardiologia, Azienda Istituti Ospitalieri, Cremona; [10]A.O. San Camillo, Cardiologia 1, Roma; [11]Oncologia Medica, Azienda Ospedaliera, Perugia

Background. Adjuvant trastuzumab, concurrent or after chemotherapy, resulted in significant increases of both DFS and OS in HER2+EBC patients.

Anthracyclines, taxanes and trastuzumab haven't potential nephrotoxicity and dose reduction in patients with renal dysfunction is not necessary. However, renal dysfunction may make the myocardium more sensible to the insult of these agents.

Patients and methods. Clinical and echocardiographic data of 499 HER2 + EBC patients, undergone adjuvant trastuzumab at 10 Italian institutions between January 2008 and June 2009, were retrospectively analyzed. Cardiotoxicity was defined according to CTCAE-NCI-2.0. LVEF was evaluated by echocardiography at baseline and at 3-6-9-12 months during trastuzumab. At 12-month evaluation were recorded the following events: decrease >10 points% of LVEF (G1); decrease of LVEF ≥20% or below the lower limit of normality (G2); occurrence of signs and symptoms of CHF (G3).

The role of renal dysfunction on development of trastuzumab cardiotoxicity in HER2 + EBC patients was evaluated.

Results. Cardiotoxicity was recognized in 133 patients (26.7%; G1 = 20.4%; G2 = 3%; G3 = 3.2%). These patients were older (57 ± 11 vs 55 ± 11 years; p = 0.03), had lower glomerular filtration rate (GFR) (76 ± 15 vs 83 ± 19 mL/min/1.73 m^2; p = 0.003) and LVEF at baseline (69 ± 6 vs 63 ± 5%; p <0.001) and received more frequently doxorubicin (18 vs 9%; p = 0.01) than patients who did not experience cardiotoxicity. Sixty percent of cardiotoxic events occurred during the first 3 months of follow-up. At univariate analysis renal dysfunction was strongly associated with events. ROC analysis showed the best cut-off point of GFR for predicting cardiotoxicity: 82 (AUC = 0.68 [95% CI 0.57-0.79]). Multiple logistic regression analysis revealed that GRF lower than 82 mL/min/1.73 m^2 was the strongest predictor of cardiotoxicity (OR3.19 [CI = 1.04-9.74]), independent of doxorubicin treatment (OR3.16 [CI = 1.06-9.39]). Lowered LVEF from baseline to 3-month follow-up was predicted by a reduced GFR (ß = 0.23, p = 0.003), doxorubicin treatment (ß = 0.16, p = 0.03) and lack of combined treatment ACEi + betablockers (ß = 0.29, p <0.001).

Conclusion. In HER2 + EBC treated with adjuvant trastuzumab, risk factors for developing cardiotoxicity at 12-month were renal dysfunction and pretreatment with doxorubicin. Therapy with ACEi and betablockers seems to confer a protective effect.

A21 SEXUALITY, EMOTIONS AND SELF-IMAGE IN WOMEN WITH BREAST CANCER

Marredda S., Sanna V., Cuccu A., Contu M., Masala A., Cucca A., Olmeo N., Contu A.

Medical Oncology, Hospital of Sassari

Background. It is widely recognized that breast cancer and its treatment have a negative impact on female sexual health, usually evaluated as disturbance in sexual function, as well as disruption of sexual arousal, lubrication, orgasm, sexual desire, and sexual pleasure.

Despite the integral role sexuality plays throughout the continuum of breast cancer, the sexual needs of a woman with breast cancer are very rarely addressed in the clinical setting.

The purpose of this study is to describe the sexual functioning concerns of breast cancer women, (BCW) in relation to age and type of treatment.

Methods. Sixty-eight BCW diagnosed with breast cancer at age 30-65, were asked to complete the following questionnaires: a) a semi-structured interview for sexual life evaluation; b) an emotional questionnaire to investigate the presence of: fear, anger, sadness and joy; c) a self-descriptive questionnaire ANINT (Benjamin-Scilligo, 2003) to measure self-image in their own daily life, according to two dimensions: affiliation (self-love vs self-attack) and interdependence (self-control vs let self emancipate).

Results. The occurrence of sexual problems was 59%; 11% of patients had experienced sexual difficulties before they developed cancer, 30% stated that their sexual life had not changed. According to the emotional questionnaire, fear, sadness and anger were noted in 70% of patients; 28% of patients had experience of happiness and 2% described other emotions. ANINT highlights how 76% of women feel self love, 15% self-control, 2% self-attack, 7% live a conflict between self-love and self-attack while 1% was not classified.

Conclusion. During chemotherapy and hormonal treatment, BCW experience poorer sexual functioning, and clinicians should inquire about these problems to provide both psychological and symptomatic management. Contrary to the expected, a great number of women describe themselves in a loving attitude. Psychotherapy is recommended in order to lower the psychological discomfort and to improve women sexual life.

A22 COMPLIANCE OF LONG-TERM ORAL CHEMOTHERAPY IN METASTATIC BREAST CANCER (MBC): THE WOMEN'S POINT OF VIEW. FINAL RESULTS OF A PROSPECTIVE ANALYSIS

Palumbo R.[1], Strada M.R.[2], Riccardi A.[3], Bernardo A.[1], Teragni C.[1], Poggi G.[1], Sottotetti F.[1], Tagliaferri B.[1], Bernardo G.[1]

[1]Operative Unit of Medical Oncology II, [2]Operative Unit of Rehabilitative Oncology, [3]Department of Medical Oncology, University of Pavia, Fondazione Salvatore Maugeri-IRCCS, Pavia

Background. Our Group had previously reported results of two consecutive phase II trials in women given full-oral CT with vinorelbine (VNR) and capecitabine (CAP) in combination (88 patients) or sequentially (46 patients) as first-line treatment of their MBC (Ann Oncol 2010; Clin Breast Cancer 2011). Here we present the final results of the prospective analysis focused on treatment compliance and tolerability.

Patients and methods. Median number of cycles administered was 12 (range 9-18). Quality of Life (QoL) was assessed every two cycles using the EORTC QLQ-BR23 questionnaire. Treatment tolerability was assessed by both the women and their physicians through a quantification of their opinion as insufficient-satisfactory-good-very good (score 0 to 3); a comparison was performed between the patient's last breast cancer therapy and the ongoing all oral regimen.

Results. Over 90% of patients and physicians rated the tolerability of full oral chemotherapy as 'very good' or 'good' throughout the study, with a slight higher physician-detected score. An improvement in tolerability was reported by 76% of patients from their last therapy to present chemotherapy: median scores changed from 1 to 2 in 41% and from 2 to 3 in 45% of cases, respectively. Tolerability at 4th and 6th cycle was also positively associated with better progression-free survival ($p = 0.02$). A statistically significant difference was observed regarding some aspects of QoL, as body image ($p = 0.02$), sexual functioning ($p = 0.01$) and future perspectives ($p = 0.03$). Oral treatment was perceived as advantageous by 98.5% of women, because of reduced hospital admissions (73.8%) and feeling of 'freedom' deriving from the home-based therapy (16.6%).

Conclusions. Our data confirm the good compliance of oral CT throughout a long-term treatment. The most interesting finding was the observed significant impact of each degree of improvement in tolerability on the clinical outcome. In our opinion this association may be partly attributable to the correlation between compliance and total number of received cycles.

A23 EFFECTS OF BODY MASS INDEX (BMI) ON PLASMA LEVELS OF ESTRONE SULFATE (ES) IN POSTMENOPAUSAL WOMEN WITH BREAST CANCER (BC) DURING LETROZOLE (L) TREATMENT

Sini V.[1], Lunardi G.[1], Del Mastro L.[2], Bighin C.[2], Marroni P.[2], Piccioli P.[2], Bisagni G.[3], Driol P.[4], Garrone O.[5], Ponzone R.[6], Porpiglia M.[7], Venturini M.[1]

[1]Ospedale Sacro Cuore-Don Calabria, Negrar (VR); [2]Istituto Nazionale per la Ricerca sul Cancro, Genova; [3]Arcispedale S. Maria Nuova, Reggio Emilia; [4]A.O.U. Santa Maria della Misericordia, Udine; [5]Ospedale S. Croce e Carle, Cuneo; [6]Institute for Cancer Research and Treatment, Candiolo (TO); [7]Ospedale S. Anna, Torino

Backgrounds. BMI is associated with an increased risk of BC in postmenopausal women. Moreover, BC overweight women have poorer prognosis compared to women with normal weight. Data from ATAC (the Arimidex, Tamoxifen Alone or in Combination study) trial reported that obesity reduces the efficacy of the aromatase inhibitor (AI) anastrozole in early BC. One possible explanation is that higher estrogens levels resulting from high BMI may lead to lower efficacy of the AI treatment. No clear data are available about the effects of BMI on estrogen circulating levels during AI treatment, and if the increase of AI dosage may result in more complete estrogen suppression in overweight women.

Methods. We evaluated the correlation between BMI and plasma concentration of ES in postmenopausal women with early BC during adjuvant treatment with L (2.5 mg/die). Patients were participating in two prospective Italian clinical trials (GIM4 and GIM5) evaluating L treatments after adjuvant tamoxifen. Plasma samples were obtained after at least six weeks of L therapy. After a non-chromatographic cleaning procedure of samples, plasma ES levels were evaluated by RIA. Ln values for plasma ES were used for statistics. Geometric means and 95% confidence interval (CI) were used as summary measures.

Results. ES plasma concentration and BMI were evaluated in 370 women. Median treatment duration was 49 wks (range 6-201 wks). Median age of patients was 60 yrs (range 34-84 yrs). Table shows data regarding ES concentrations and BMI of patients.

BMI, kg/m^2	No. of pts	%	ES geom mean (pg/mL)	95% CI
<230	85	23	21.7	21.2-22.5
2.30-24.9	65	18	20.2	19.6-20.9
2.50-27.9	111	30	24.2	23.8-24.6
2.80-29.9	43	12	22.5	21.5-23.6
>30.0	66	17	19.8	19.2-20.4

Conclusions. Circulating ES levels during L (2.5 mg/die) treatment were superimposable in all BMI groups. Our data indicate that whether BMI influences AI efficacy, this is not due to an insufficient suppression of aromatase activity in women with higher BMI. Increasing the dose of AI to further reduce ES levels in high BMI patients is a questionable way to increase AI efficacy.

A24 TOPOISOMERASE II ALPHA (TOPOIIA) AND MAPTAU: POTENTIAL PREDICTIVE MARKERS OF RESPONSE IN LOCALLY ADVANCED BREAST CANCER (LABC) TREATED WITH NEOADJUVANT EPIRUBICIN AND DOCETAXEL (ET) IN NEOADJUVANT SETTING

Cristofano A.[1,2], Arena V.[3], Inno A.[1], Nicosia L.[1], Jocolle G.[2], Carassai P.[4], Schinzari G.[1], Basso M.[1], Bagalà C.[1], Numico G.[2], Barone C.[1]

[1]Divisione di Oncologia Medica, Università Cattolica del Sacro Cuore, Roma; [2]Struttura Complessa Oncologia, Ospedale "U. Parini", Aosta; [3]Istituto di Anatomia Patologica, Università Cattolica del Sacro Cuore, Roma; [4]Anatomia Patologica, Ospedale "U. Parini", Aosta

Background. Some findings have already suggested that TopoIIa over-expression may be a predictive marker of response to anthracyclines. Since MAPtau regulates the activity of microtubules, which are targeted by taxanes, the level of expression of MAPtau may probably influence the activity of these drugs.

Methods. TopoIIa and MAPtau expression was evaluated by immunohistochemistry (IHC) in tumour biopsy from 22 women

with LABC receiving ET as neoadjuvant chemotherapy, and protein levels were correlated to the outcome.

Results. TopoIIa and MAPtau were over-expressed in the same percentage of tumours (38.9%), but there was no significant correlation between the two proteins. TopoIIa over-expression was significantly associated with ductal histology (58.3% in ductal carcinoma vs 0% in other hystotypes, p = .038) and hormone receptors (HRs) expression (63.6% in positive vs 0% in negative tumours), whereas no significant correlation was observed with HER2 expression. MAPtau did not correlate with histology, grading, HRs and HER2 status. Pathological complete response (pCR) rate was higher in MAPtau low/normal expressing tumours when compared with those over-expressing the protein (36.4% vs 14.3%), even not significantly. Patients with TopoIIa over-expression achieved a significantly higher pCR rate than those with a low/normal expression (57.1% vs 9.1%; p = .047). Median Relapse-Free Survival (RFS) was 36 months; for pts who achieved a pCR, the median RFS has not been reached yet. Ductal histology and HR expression were associated with a longer RFS (ductal vs other histology: 44 vs 18 months; p = .045; HR positive vs negative tumours: 77 vs 18 months; p = .0028). Instead, TopoIIa and MAPtau expression, grading and HER2 status did not correlate with RFS.

Conclusions. IHC evaluation of TopoIIa and MAPtau might be useful in identifying pts potentially responsive to neoadjuvant chemotherapy with anthracyclines and taxanes. However, these results need to be prospectively confirmed in a larger series.

A25 OUTCOME OF EARLY BREAST CANCER (EBC): OUR EXPERIENCE

Latiano T.P.[1], D'Addetta C.[1], Parrella P.[2], Di Micco C.[1], Murgo R.[3], Piano A.[1], Morritti M.[1], Valori V.M.[1], Castelvetere M.[4], Lombardi L.[1], El Jaouni M.[5], Copetti M.[5], Fontana A.[5], Maiello E.[1]

[1]Oncology Unit, [2]Oncology Laboratory, [3]Surgery Unit, [4]Pathology Unit, [5]Radiotherapy Unit, [6]Unit of Biostatistics, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, FG

Background. The frequency of stage I (T1a, b) node negative invasive breast cancers (BC) is increasing because of wider implementation of breast cancer screening. Most of the existing literature on the subject is retrospective and shows variability in the prognosis of these patients, with a disease-free survival (DFS) range of 79-98%. The aim of the present study was to analyze the DFS in our cohort and their correlation to clinico-pathological prognostic factors (age, tumour size, histological grade, hormone receptor and HER-2 expression, fertility, and systemic adjuvant therapy).

Methods. Two hundred and forty-eight patients with early breast cancer (pT1a, b N0M0) were observed between March 1996 and December 2010 (median follow-up 73 months IQR 44-112) and were retrospectively investigated in our Institution. Tumours were classified histologically according to the World Health Organization Histological classification on breast cancer. Tumour grading was assessed according to Elston and Ellis. Estrogen Receptor (ER) and Progesteron Receptor (PgR) status and HER2neu overexpression were evaluated immunocitochemically. The threshold for ER and PgR positivity was 10%

Results. Of the 248 cases, 60 tumours (25%) were classified as pT1a, and 188 tumours (75%) were classified as pT1b. The main characteristics of these pts included: median age 54 years; positivity history family cancer: specific 59 pts (24%); menopause 147 pts (60%); fertility 164 pts (66%); surgery: mastectomy 34 pts (14%) and local excision 214 pts (86%). Progesterone receptor was positive in 70% of all cases and 75% ER-positive. HER2 status was also determined on a subset of the 94 pts (38%). Overall, 75% of pts affected by EBC received hormonal therapy and 25% received chemotherapy. The 5 years DFS was 96%. Twelve patients experienced disease progression, of those 6 showed local recurrence and the remaining 6 distant metastases. Univariate analysis demonstrated an association between ER and PR status and tumour grade (p = 0.005) and ki67/mib1 expression (p = 0.001). In Kaplan-Meier analysis, only HER2 neu status was associated with disease free survival (Long Rank Test p = 0.005).

Conclusions. Although the overall prognosis of patients with early stage breast cancer is excellent, we observed that the HER2neu status was a predictor of worst DSF.

A26 IDENTIFICATION OF TISSUE MARKERS FOR THE PREDICTION OF BONE METASTASES IN BREAST CANCER PATIENTS

Mercatali L., Ibrahim T., Scarpi E., Guerra D., Liverani C., Ciani S., Amadori D.

Osteoncology Center, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), Meldola (FC), Italy

Background. The bone metastasization process comprises numerous steps, i.e. proliferation, invasion and adhesion, involving molecules, growth factors, chemokines and their receptors, which confer the bone-like phenotype. Thus, only cancer cells with specific features are capable of reaching and colonizing bone tissue. Timely prediction of relapse to bone could be used to select patients for tailored therapy with bone-specific drugs such as bisphosphonates or RANK-L inhibitors.

Methods. We retrospectively evaluated TFF1, DKK1, IBSP, HPSE, SPP1, Agr2, SPARC, CTGF, COMP, FST, and RANK transcript levels by quantitative Real-Time PCR in fresh and frozen breast cancer tissue from 40 patients to predict risk and site of relapse. Fifteen patients had bone metastases (BMP), 10 visceral metastases (VMP), and 15 no evidence of disease (NEDP). The predictive accuracy of each marker was calculated using Receiver Operating Characteristic (ROC) curves.

Results. Median values of each marker were calculated for each subgroup: TFF1 median values were about 7-fold higher in BMP than in either control group (VMP-NEDP) (p = 0.05); COMP and HPSE median values were about twice as high in BMP as those in NEDP and VMP groups. The area under the curve (AUC) was 0.73 for TFF1 and 0.62 for HPSE and COMP. Considering markers as dichotomous variables, TFF1 expression reached 67% in BMP compared to 21% and 20% in NEDP and VMP, respectively. TFF1 was also analyzed in association with other markers and, for the combination of TFF1, DKK1, and IBSP, 80% expression was observed for the BMP group, whereas low expression levels were maintained in both control groups (21% and 20%, respectively) (p = 0.041).

Conclusions. Our preliminary results indicate that the combined analysis of TFF1, DKK1 and IBSP expression in primary breast tumours could be useful to identify patients at high risk of bone relapse as potential candidates for adjuvant preventive

bone-specific therapy. Confirmation of results is now needed in larger case series.

A27 PHASE I-II STUDY WITH THE FULL-ORAL METRONOMIC SCHEDULE OF VINORELBINE (VNB) AND CAPECITABINE (CAPE) IN METASTATIC BREAST (MBC) CANCER PATIENTS: PRELIMINARY RESULTS OF EFFICACY AND TOXICITY. THE VICTOR-1 STUDY

Cazzaniga M.E.[1], Torri V.[2], Villa F.[1], Giuntini N.[1], Zeppelini A.[1], Riva F.[1], Cortinovis D.[1], Bidoli P.[1] on behalf of The VICTOR Study Group

[1]S.C. Oncologia Medica, A.O. S. Gerardo, Monza; [2]Istituto M. Negri, Milano

Background. Different studies have demonstrated the efficacy of VNB and CAPE in the clinical control of MBC patients (pts). We recently presented (Cazzaniga ME, SABCS 2010 #P6) the results concerning the phase I part of the VICTOR study, which has established the MTD of VNB in combination with fixed continuous doses of CAPE (500 mg/day, tid) as 40 mg/day thrice a week. All pts who reached the MTD of VNB without G3/4 adverse events continued to be treated with the combination until progression, unacceptable toxicity or refusal to receive the treatment, to confirm the toxicity profile and to preliminarily assess the clinical activity. Preliminary data of efficacy and toxicity are presented.

Patients and methods. From October 2009 till April 10, we enrolled 12 pts in the phase I part and 19 pts in the phase II one. Pts with MBC, HER2-, or HER2+ but no more suitable to anti-HER2 agents disease, previous treatment with anthracyclines and taxanes, measurable or evaluable disease according to RECIST 1.1 criteria have been treated with VNB 40 mg/tot, days 1, 3, 5 and CAPE 500 mg/day, tid. Biological characteristics of the pts were: HR+ 77.4%, HER2- 73%; 19 pts (61.3%) had received 1 or more treatments for the metastatic disease. The vast majority of the pts (78%) had ≥2 metastatic sites. ECOG PS was 0-1 in 67% of the pts.

Results. Median age was 73 years (47-84). At the moment of this analysis, 23 pts are evaluable for the clinical response and 19 for the Clinical Benefit (CB = CR + PR + SD ≥24 weeks). The best response was PR in 8/23 (35%) pts and SD in 10 (43%). CB was obtained in 11/19 pts (57.9%) and in the 54% of the CHT-pretreated pts. We described 6 G ≥3 events (G3 = 4: anaemia, diarrhoea, paresthesiae, and hand-foot syndrome; G4 = 2: neutropenia) considering a total of 183 cycles. The G4 events required treatment discontinuation.

Conclusion. These preliminary results indicate that the full-oral combination of VNB and CAPE is active also in heavily pretreated MBC pts with bulky disease, with an acceptable toxicity profile and could represent a valid therapeutic option for the disease control.

A28 PILOT STUDY OF CORRELATION BETWEEN SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) OF PRO- AND ANTI-ANGIOGENIC GENES AND RESPONSE TO BEVACIZUMAB (BV) PLUS CHEMOTHERAPY (CT) IN PATIENTS WITH METASTATIC BREAST CANCER (MBC)

Allegrini G.[1], Bocci G.[2], Fontana A.[12], Amoroso D.[6], Ferro A.[3], Giuntini N.[4], Casadei V.[5], Di Lieto M.[7], Marcucci L.[1], Pazzagli I.[8], Coltelli L.[9], Lucchesi S.[1], Arrighi M.[10], Scalese M.[11], Camerini A.[6], Orlandi P.[2], Bona E.[12], Villa F.[4], Di Pasquale M.[3], Falcone A.[12]

[1]U.O. Oncologia Medica, Az-USL5 di Pisa; [2]Divisione di Farmacologia e Chemioterapia, Dipartimento di Medicina Interna, Università di Pisa; [3]U.O. Oncologia Medica, Ospedale "S. Chiara", Trento; [4]Struttura Complessa di Oncologia Medica, A.O. San Gerardo, Monza; [5]U.O. Oncologia Medica, AOR Marche Nord, Pesaro; [6]U.O. Oncologia Medica, Ospedale Versilia, Azienda USL12, Lucca; [7]Sezione Oncologia Medica, Ospedale Del Ceppo, Pistoia; [8]U.O. Oncologia Medica, Ospedale SS. Cosma e Damiano, Pescia (PT); [9]Presidio Ospedaliero Elba, Az. USL6, Livorno; [10]U.O. Chirurgia Generale, Az-USL5 di Pisa; [11]Istituto di Fisiologia Clinica, CNR, Pisa; [12]U.O. Oncologia Medica II Universitaria, Polo Oncologico, Ospedale S. Chiara, AOUP, Pisa

Three phase III trials demonstrated an increase of activity and PFS of BV + CT in MBC patients but not of OS compared to CT alone (Miller 2007, Miles 2010, Robert 2011). Predictive biomarkers of response to BV are highly needed. Schneider et al. (JCO 2008) investigated the role of somatic, multiple VEGF SNPs as predictors of pts outcome to BV + paclitaxel. Final results showed a greater OS for the combination when VEGF-2578 AA and VEGF-1154 AA genotypes were expressed. On the basis of these promising results, we decided to conduct a retrospective analysis in a MBC population treated with BV + CT with the aim to investigate a possible correlation between different VEGF, VEGFR-2, IL-8, IL-6 and TSP-1 genotypes and outcome of pts treated with BV plus CT. Analyses were performed both on germline and somatic DNA. The study is still ongoing and, up today, 68 patients treated with first line BV + paclitaxel have been enrolled from 10 Oncology Units in Italy. Main pts characteristics are: median age of 57 years (range 33-80), ECOG-PS of 0/1 in 78%/22% of pts, sites of disease single/multiple in 34%/66% of pts. Among 53 pts evaluated for response, 35 partial and 4 complete response for a total RR of 71.7% 95% (CI: 52.2%-84.2%) were observed. After a median follow-up of 22.5 months, median PFS is 10.5 months (range 3.5-36+) and median OS has not been reached. Germline SNP analyses of these genes have been performed on 48 blood DNA samples. Preliminary results have shown a high frequency of VEGF-1154 AA genotype (54.8%) that has been described to correlate with the best probability of OS in the Schneider's study (mOS of 46.5 months). Correlations with patients outcome will be performed with a greater number of events and of patients enrolled, expected by the annual meeting.

Study supported by the no-profit foundations F.A.R.O. and A.R.C.O.

A29 ORMONORESPONSIVE BREAST CANCER. THE PREDICTIVE ROLE OF GENETIC POLYMORPHISM IN THE AROMATASE GENE

Cattaneo M.T., Clementi E.*, Pellegrino P., Cattaneo D.*, Radice S.*, Filipazzi V., Somma L., Farè E., Tosca N., Isabella L., Gambaro A., Ferrario S., De Troia B., Damiani E., Piazza E.

*Oncology Department, *Pharmacology Department, "Luigi Sacco" Hospital, Milan*

Introduction. Aromatase inhibitors are the milestone of endocrine therapy in postmenopausal breast cancer[1]. Aim of this study was to evaluate the treatment efficacy of third generation aromatase inhibitors, anastrozole, letrozole and exemestane, in breast cancer patients segregated whit respect to DNA polymorphism of aromatase gene CYP19A1 (rs4646).

Methods. We analyzed 116 consecutive postmenopausal women whit breast cancer ER/PgR [+] treated with aromatase inhibitor. Genotypes from blood were retrospectively evaluated by real time PCR followed by Pyrosequencing. The rs4646 SNP analyzed is located in the 3' untranslated region. Response to therapy was evaluated whit radiological, clinical and biochemical markers.

Results. Ninety patients were treated in adjuvant regime, 26 were treated for metastatic disease Median age was 69.3 years. Genotype frequencies show a 58% for wild type (C/C), 32% for heterozygous (C/A) and 10% for homozygous (A/A). We found a correlation between homozygous genotype and poor response to exemestane ($p = 0.018$) in metastatic disease. No evidence correlation was instead observed between poor response and this polymorphism and anastrozole and letrozole.

Conclusion. This analysis demonstrates the significant influence of rs4646 gene polymorphism in response in exemestane therapy for breast cancer disease. Pharmacogenetic analysis can potentially allow the creation of patient-tailored therapy.

References

1. Doyen J et al: Aromatase inhibition in breast cancer patients: biological and clinical implications. Ann Oncol, 21 (6): 1243-1245, 2010.

A30 FULVESTRANT ADMINISTERED IN TWO DIFFERENT SCHEDULES: PHARMACOKINETICS, BIOLOGICAL MARKERS AND ACTIVITY

Felici A.[1,3], Naso G.[2], Di Segni S.[3], Vici P.[4], Antenucci A.[5], Angelini F.[6], Pizzuti L.[4], Mandoj C.[5], Cognetti F.[1], D'Auria G.[7], Fabi A.[1], Tata A.[3], Papaldo P.[1]

[1]Division A of Medical Oncology, Regina Elena Cancer Institute, Rome, Italy; [2]Division of Medical Oncology, Policlinico Umberto I, Rome, Italy; [3]Laboratory of Pharmacokinetic, Regina Elena Cancer Institute, Rome, Italy; [4]Division B of Medical Oncology, Regina Elena Cancer Institute, Rome, Italy; [5]Clinical Pathology, Regina Elena Cancer Institute, Rome, Italy; [6]Medical Oncology, Regina Apostolorum, Albano Laziale, Italy; [7]Medical Oncology, Belcolle Hospital, Viterbo, Italy

Background. Fulvestrant (F) had a proved efficacy as second-line endocrine therapy in menopausal patients with hormone-responsive metastatic breast cancer (HR-MBC). At 250 mg/monthly the plasmatic concentration reached the steady state after 3-6 doses. In addition, F has been shown to induce the tissue factor pathway of coagulation.

Methods. We analysed activity, pharmacokinetics (PK) and markers of coagulation and angiogenesis of F administered in two different schedules in HR-MBC women progressing after a first-line treatment. In schedule A, a high dose was administered in the first 3 months (500 mg on days 0, 14, 28, then at 250 mg every 2 weeks for 5 administrations, then at 250 mg every 28 days); in schedule B a standard dose was administered (250 mg every 28 days). The serum level of VEGF (sVEGF/pVEGF), and procoagulant factors, such as tissue factor, thrombin/antithrombin complex, and prothrombin fragments 1+2, was determined, by ELISA, before each drug administration. In addition a PK analysis, by HPLC-MS/MS, was carried out to determine the PK of F in the two arms.

Results. In this ongoing multicenter study, 38 patients were included: 23 in arm A, and 15 in arm B. Median age was 63 (45-86); 17 and 22 patients received a prior line of chemotherapy and hormone-therapy respectively. Of the 31 evaluable patients: one had a partial response in arm A, 7 and 3 pts had stable disease in arm A and B respectively, and 20 patients progressed (10 in each arm). A high baseline value of coagulation markers and angiogenesis characterized all patients. A reduction of serum VEGF levels during therapy was observed, while procoagulant factors remained stable. At day 28, the mean plasma concentration of F was 18.22 ng/mL and 6.43 ng/mL in arm A and B, respectively. The drug steady state was reached in the experimental arm after 28 days.

Conclusions. Even if preliminary, these results show that, in the high dose arm, plasma concentration of F was more than double after only one month of therapy, while circulating levels of VEGF were lower. Furthermore, in the same arm compared with control, an increase of stable disease was achieved in second-line setting patients.

A31 INHIBITION OF CANCER CELL GROWTH AND INVASION BY TARGETING C-SRC IN BREAST CANCER MODELS RESISTANT TO ANTI-HER2 DRUGS

Formisano L.[1], Damiano V.[1], Nappi L.[1], Rosa R.[1], Gelardi T.[1], D'Amato C.[1], Marciano R.[1], De Maio A.P.[1], Ferrara R.[1], Tortora G.[2], Veneziani B.M.[3], De Placido S.[1], Bianco R.[1]

[1]Dipartimento di Endocrinologia e Oncologia Molecolare e Clinica, Laboratori di Terapia Medica dei Tumori, Università Federico II, Napoli; [2]Cattedra di Oncologia Medica, Università di Verona; [3]Dipartimento di Biologia e Patologia Cellulare e Molecolare "L. Califano", Università Federico II, Napoli

Background. Inhibition of the HER2 tyrosine kinase receptor represents one of the most successful approach in breast cancer management. Both monoclonal antibodies, such as trastuzumab, and small tyrosine kinase inhibitors, such as lapatinib, possess considerable clinical efficacy in certain patients with HER2-overexpressing breast cancer (BC). However, overall response rate to these drugs remains modest, many patients do not respond to primary treatment and almost all of responders develop resistance after continuous exposure. Recently, activation of c-Src tyrosine kinase has been related to resistance to HER2 inhibitors and drugs against c-Src are currently in early phases of clinical development.

Experimental plan. We selected human BC cell lines sensitive or resistant to trastuzumab or lapatinib. On these models we evaluated antitumour, antiangiogenic and antimetastatic activity of the c-Src inhibitor saracatinib, alone or in combination with HER-2 inhibitors, both *in vitro* and *in vivo*.

Results. We demonstrated that saracatinib inhibits *in vitro* growth and survival of BC cell lines, both sensitive or resistant to trastuzumab or lapatinib. Moreover, saracatinib is able to interfere with migration and invasion capabilities of BC cells, as

demonstrated with specific assays. These effects correlate with a direct antiangiogenic activity, since saracatinib treatment interferes with survival, migration and capillary tubes formation in HUVEC cells. In addition, perturbations in cancer cell invasion induced by saracatinib are associated to reduced phosphorylation of Src transducers such as FAK and paxillin as well as other signaling molecules. When combined with lapatinib or trastuzumab, saracatinib produces a strong cooperative effect in inhibiting migration and invasion, even in resistant cells. We are now evaluating the effects of saracatinib, alone or in combination with lapatinib or trastuzumab, on *in vivo* invasiveness of BC cell lines, through spontaneous and artificial metastasis assays.

Conclusions. We demonstrated that saracatinib, alone or in combination with HER-2 inhibitors, is effective in human BC models both sensitive and resistant to trastuzumab or lapatinib, inhibiting cancer cell growth and invasion capability.

A32 OMISSION OF AXILLARY DISSECTION AFTER A POSITIVE SENTINEL NODE BIOPSY FOR BREAST CANCER: POTENTIAL IMPLICATIONS ON THE PRESCRIPTION OF ADJUVANT CHEMOTHERAPY

Montemurro F.[1], Maggiorotto F.[2], Valabrega G.[1], Kubatzki F.[2], Rossi V.[1], Marocco F.[2], Magistris A.[2], Aglietta M.[1], Ponzone R.[2]

[1]Division of Medical Oncology, [2]Division of Gynecological Oncology, Institute for Cancer Research and Treatment, Candiolo, Italy

Introduction. A recent study indicates that axillary dissection (AD) may be avoided in breast cancer (BC) patients with a clinically negative axilla and a positive sentinel lymph node (SLN) biopsy receiving breast conserving surgery (BCS) (JAMA 2011; 305: 569). Because the number of positive axillary lymph nodes (ALN) is a prognostic marker, we studied how omission of AD could affect the indication to adjuvant chemotherapy (ACT).

Patients and methods. Among 1497 patients operated over 10 years, we identified 328 patients with cT1/2 cN0 breast cancer submitted to BCS and with 1 to 3 positive SLN(s) (median 1, range 1-3). All patients underwent AD. Each case was reviewed by our breast team in two rounds. Patient age, histopathology, tumor biomarkers and number of positive SN nodes (micro and/or macrometastatic) were available in the first round. In the second, the information on ALN was added. At each round, the panel chose between three indications: 1) recommend ACT; 2) discuss ACT; 3) no ACT.

Results. SN was micrometastatic in 148 (45%) and macrometastatic in 180 patients (55%). Metastases in non-SNs were found in 99 patients (30%), including 55 with ≥4 positive ALN (range 4-24). First round results: recommend ACT in 182 (56%), discuss ACT in 63 (19%), no ACT in 83 (25%) patients. Second round results: recommend ACT in 213 (65%), discuss ACT in 50 (15%), no ACT in 65 (20%) patients. No change in the initial decision occurred in 275 patients (84%). The most frequent change was a recommendation to ACT (36 patients, 11%). Most of the changes (42 pts, 20%, p = 0.05 for comparison with other subgroups) occurred in patients with Luminal B/HER2 negative breast cancer (ER+ and Ki67 ≥14%) and were towards ACT.

Conclusions. Omission of AD in patients with a positive SLN receiving BCS would have altered the indication to ACT in 16% of the patients at our Institution. The implications of such policy must be taken into account before its widespread acceptance.

A33 FEASIBILITY OF ADJUVANT TRASTUZUMAB FOR HER2-POSITIVE (HER2+) EARLY BREAST CANCER (EBC) PATIENTS WITH INCREASED CARDIOVASCULAR RISK: ECHOES FROM "REAL WORLD"

Ceccherini R.[1], Tuccia F.[2], Laveder F.[2], Russo G.[3], Lestuzzi C.[4], Simoncini E.[5], Faggiano P.[6], Nunzi M.[7], Sabatini S.[7], De Bonis P.[8], Anastasi P.[9], Gori S.[9]

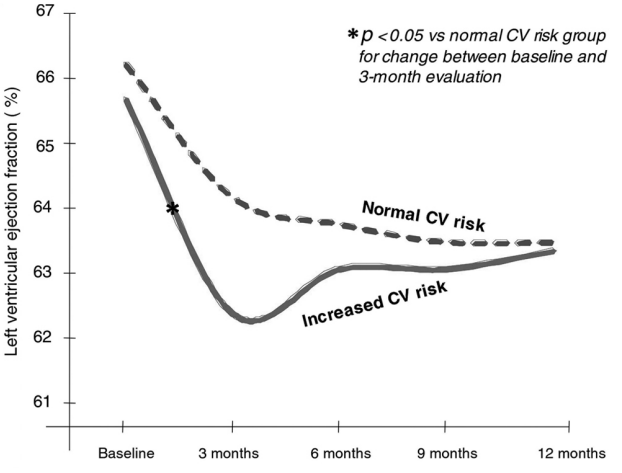
[1]A.S.S. n. 1, Centro Sociale Oncologico, Trieste; [2]ASL1 Veneto, Unità Operativa di Oncologia, Ospedale San Martino, Belluno; [3]A.S.S. n.1 Centro Cardiovascolare, Trieste; [4]CRO, National Cancer Institute, Department of Cardiology, Aviano; [5]Oncologia Medica, A.O. Spedali Civili di Brescia; [6]Dipartimento di Cardiologia, A.O. Spedali Civili di Brescia; [7]Oncologia Medica, A.O. Terni; [8]Cardiologia, A.O. Terni; [9]Dipartimento di Oncologia, Perugia

Background. Adjuvant trastuzumab in HER2+ early breast cancer exposes patients to risk of heart failure development. High cardiovascular (CV) risk patients are under-represented in randomized clinical trials.

Patients and methods. Between 2008 and 2009, 499 HER2+EBC were treated at 10 Italian institutions with adjuvant trastuzumab. We evaluated: 1) the feasibility of adjuvant trastuzumab in high CV risk patients; 2) if the management of CV risk factors may influence the trastuzumab-cardiotoxicity. Cardiotoxicity was defined according to CTCAE-NCI-2.0

A probability >5% of cardiac events in the following 10 years according to the score of European Society of Cardiology (ESC) was the definition of high CV risk. At 12-month evaluation, any occurrence of symptoms of CHF and/or decrease >10 points% of left ventricular ejection fraction (LVEF) were recorded.

Results. Seventy-seven out of 499 patients (15.4%) presented a high CV risk. They were older (63 ± 8 vs 54 ± 11 years), more frequently with hypertension (79 vs 17%, p <0.01), diabetes (35 vs 0%, p <0.01), dyslipidemia (66 vs 5%, p <0.01), current smokers (34 vs 12%, p <0.01) and with a history of coronary artery disease (10 vs 0%, p <0.01) than those with low CV risk. The former received more frequently ACE-inhibitors/ARBs (53 vs 12%), betablockers (38 vs 7%), and statins (32 vs 3%) than the latter. Chemotherapy did not differ between the two groups. Although pts presented similar LVEF at baseline (65 ± 7 vs 65 ± 6%) and at 12-month evaluation (63 ± 6 vs 63 ± 6%, both p = ns), high CV risk patients presented a significant early reduction of LVEF (Figure).



Conclusion. Patients at increased cardiovascular risk are 15.4% of patients treated with adjuvant trastuzumab. Early cardiotoxicity was observed more frequently in these patients. A pharmacological management of traditional cardiovascular risk factors seems to confer a protective effect and consent to complete the chemotherapy.

A34 PHARMACOGENETICS OF CAPECITABINE-BASED TREATMENT IN ADVANCED BREAST CANCER PATIENTS

Cappelletti M.R., Foroni C., Maldotti M., Andreis D., Bazzola L., Strina C., Bertoglio P., Milani M., Bottini A., Generali D.

U.O. Multidisciplinare di Patologia Mammaria, A.O. Istituti Ospitalieri, Cremona

Background. Genes for which polymorphisms may potentially influence inter-individual pharmacodynamics variation of fluoropyrimidines, including capecitabine, are the methylenetetrahydrofolate reductase (MTHFR), and the dihydropyrimidine dehydrogenase (DPD). The aim of this pilot study was to analyze the effect of MTHFR and DPD single nucleotide polymorphisms (SNP) on toxicity in advanced breast cancer patients (pts) receiving capecitabine-based treatment.

Patients and methods. Nineteen pts (median age 58.8 years, ECOG-PS 0-3) were initially treated with capecitabine 1500 mg (53%) or 2000 mg (47%) daily in a metronomic fashion, alone (10%) or associated with vinorelbine (90%). Genomic DNA was isolated in peripherical blood. DPD SNP (IVS14 + 1G >A) and MTHFR SNPs (677C >T and 1298A >C) were investigated using Pyrosequencing platform. Data were analyzed by two-sided Fisher's exact test.

Results. Treatment was well tolerated; the most frequent toxicities, evaluated with the NCI-CTCAE v3.0, were hand-foot skin reaction (42%), hematotoxicity (42%), diarrhea (21%) and nausea-vomiting (16%). MTHFR677C >T SNP was detected in 12 pts (63%), 4 homozygous and 8 heterozygous; MTHFR1298A >C SNP in 11 pts (58%), 1 homozygous and 10 heterozygous; no detection of DPYDIV14 + 1G >A SNP were found. A trend toward a higher global toxicity grade 2-4 was observed in pts homozygous or heterozygous for the MTHFR1298A >C compared with wild-type pts (100% vs 63% respectively; $p = 0.058$). We found a significant association (91% vs 38%; $p = 0.041$) between heterozygous or homozygous variant genotypes at MTHFR1298A >C and at least one management strategy of treatment-related toxicities, such as dose reduction (in 8 pts, 6 of whom were with mutation), temporary treatment interruption (in 8 pts, 7 of whom with mutation), or discontinuation (in 1 pt, with mutation).

Conclusions. The present data suggest that breast cancer pts carrying mutation for MTHFR1298A >C are not good candidates for capecitabine-based therapy, and dose modification or treatment interruption are often needed. These preliminary data require further confirmation on a larger number of patients.

A35 LOCALLY ADVANCED BREAST CANCER HER2 POSITIVE: USE OF TRASTUZUMAB IN NEOADJUVANT SETTING

Giraudi S., Bighin C., Levaggi A., Lambertini M., Iacono G., Canavese G., Pronzato P., Del Mastro L.

Istituto Nazionale per la Ricerca sul Cancro, Genova

Background. In women with HER2 positive, locally advanced breast cancer (LABC), the addition of trastuzumab to standard neoadjuvant anthracycline-based chemotherapy substantially increases the rate of pathological complete response (pCR) and the event-free survival. The potential cardiotoxicity of the concurrent use of trastuzumab and anthracycline is a major concern of such regimens. Another way to give preoperative trastuzumab is to introduce it in the second part of sequential anthracycline-taxane containing regimens, concurrently with a taxane, avoiding the concurrent use of trastuzumab and anthracycline.

Materials and methods. From July 2007 to October 2010 twenty-three patients with LABC were treated with the following neoadjuvant regimen: FEC (5-fluorouracil 600 mg/m^2, epirubicin 90 mg/m^2, cyclophosphamide 600 mg/m^2) every 3 weeks for 4 cycles followed by weekly paclitaxel (80 mg/m^2) given concurrently with trastuzumab 2 mg/kg/weekly (loading-dose: 4 mg/kg). Trastuzumab was continued after surgery for a total of 52 weeks. Cardiac evaluation included an echocardiogram or a cardiac scan performed at baseline and at the end of chemotherapy. Fifteen patients had a stage III disease and eight patients had a stage II disease.

Results. A clinical complete response was observed in 15 patients (68%) and a clinical partial response in 7 patients (32%). Clinical response was also assessed by echography, mammography or nuclear magnetic resonance (NMR) in 20 patients: a complete response was observed in 7 patients (35%) and a major partial response in 13 patients (65%). No cardiotoxic event was observed. A pCR, defined by the absence of invasive cancer both in the breast and in axilla, was observed in 19 patients (83%); in 4 cases a residual ductal carcinoma *in situ* was observed.

Conclusions. The positive results in terms of pCR in our case series, in spite of the low number of treated patients, suggest the possibility to test in adequate trials regimens in which trastuzumab was given in combination with a taxane and not with the anthracycline.

A36 SHORT DOSE-DENSE NEOADJUVANT CHEMOTHERAPY BY PEG-FILGRASTIM SUPPORT WITH EPIRUBICIN OR DOCETAXEL AND CYCLOPHOSPHAMIDE IN CLINICAL NEGATIVE AND POSITIVE AXILLARY NODE BREAST CANCER

Lipari H.[1], Catalano F.[1], Parisi A.[1], Pagano N.[1], Urso O.[1], Giovinetto R.[1], Fraggetta F.[2], Galia A.[2], Ravalli C.[1], Cannavò L.[1], La Spina S.[1], Scollo P.[1], Banna G.L [1]

[1]Division of Medical Oncology and Breast Unit, Maternal-Infant Department, [2]Service of Human Pathology, Cannizzaro Hospital, Catania, Italy

Background. To evaluate a short dose-dense neoadjuvant chemotherapy with epirubicin (E) or docetaxel (T) and cyclophosphamide (C) with pegfilgrastim support in patients with breast cancer.

Methods. In a phase II study, women with histologically confirmed diagnosis of primary breast cancer, aged 18-75 years, with

clinical stage T2-T4 and N0-N3 were treated. Patients with clinical negative axillary nodes (cN0) were treated with i.v. E 90 mg/m^2 and i.v. C 600 mg/m^2 on day 1, every two weeks (ECdd) for 4 cycles. Patients with clinical positive axillary nodes (cN+), were treated with the same regimen until September 2007. Thereafter, the protocol was amended and those patients with cN+ were treated with i.v. T 75 mg/m^2 and i.v. C 600 mg/m^2 on day 1, every two weeks (TCdd) for 4 cycles. The primary endpoint was pathological complete response rate (pCR), as defined by ypTx-0 and ypN0. Secondary endpoint was toxicity analysis.

Results. Thirty-six women, with a median age of 50 years (range 33-69) were treated. Twelve patients (33%) had cNo and were given ECdd; 8 patients (22%) with cN+ received the ECdd and 16 (44%) with cN+ the TCdd. A pCR was observed in 3 patients (25%) with cN0 treated with ECdd, in none patient (0%) with cN+ treated with TCdd, and in 1 patient (6%) with cN+ treated with TCdd. In all 36 patients, pegfilgrastim support allowed to recycle in 14 days. Three patients out of 16 (19%) who started TCdd, had to change this treatment after the first cycle for allergic reaction to docetaxel. With the exception of these three G3 toxicities, no other G3-G4 toxicities were observed.

Conclusions. A short dose-dense neoadjuvant chemotherapy is feasible with pegfilgrastim support, allows a short time to surgery, and can be used as a test of *in vivo* chemosensitivity for adjuvant chemotherapy. The ECdd may produce a good pCR rate in cN0, whilst both ECdd and TCdd seem less effective in cN+ patients.

A37 THE ROLE OF A PANEL OF MARKERS FOR THE PREDICTION OF BONE METASTASES IN BREAST CANCER PATIENTS

Ibrahim T., Mercatali L., Sacanna E., Ricci R., Scarpi E., Fabbri F., Serra P., Tison C., Liverani C., Guerra D., Ciani S., Amadori D.

Osteoncology Center, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), Meldola (FC), Italy

Background. Bone metastases are responsible for high morbidity and reduced quality of life in cancer patients. Zoledronic acid (Zometa®, Zol) represents the standard treatment for this subset of patients; although its main mechanism of action is bone resorption inhibition, it also has direct and indirect antitumour properties, e.g. antiangiogenic effects.

Methods. We prospectively evaluated RANK, RANKL and OPG transcript levels by Real-Time PCR in the peripheral blood of 49 consecutive patients with advanced breast (36), prostate (7) or lung cancer (6). Eligibility criteria included no previous treatment with bisphosphonates and first diagnosis of bone metastases. All patients received the standard Zol schedule of a 4 mg infusion every 28 days. Patients were monitored for about 12 months and blood samples were collected before the first infusion of Zol and every 4 months thereafter.

Results. Forty-nine patients had 3 blood samples taken, while 4 blood samples were taken from 29 patients. Baseline RANK, RANKL and OPG median values were 78.3 (range 7.3-620.6), 319.1 (21.4-1884.4) and 1.52 (0.1-58.0), respectively. At 12 months RANKL median value had decreased by 22% with respect to baseline, whereas OPG median value had increased by about 96%. Consequently, the RANKL/OPG ratio decreased by 56% with respect to baseline. These differences, however, did not reach statistical significance, perhaps due to the small case series evaluated. Conversely, although RANK median values had increased by 36% with respect to baseline at 8 months, they returned to near baseline values at 12 months. OPG, RANK and RANKL/OPG levels were significantly correlated with each other.

Conclusions. Ours is one of the few prospective studies to evaluate circulating markers that are potentially correlated with bone metastases. We observed that markers of the RANK/RANKL/OPG pathway in the peripheral blood of bone metastasis patients were probably modulated by Zol treatment. Zoledronic acid would appear to decrease osteoclast activity directly but also via RANK/RANKL/OPG pathway modulation. Further investigation of these biological results is warranted.

A38 RELATIONSHIP BETWEEN CHANGES IN LEFT VENTRICULAR EJECTION (LVEF) AND USE OF ANGIOTENSIN-CONVERTING ENZYME INHIBITORS/RECEPTOR BLOCKERS [ACEI/ARB AND/OR BETABLOCKERS (BB)] DURING ADJUVANT TRASTUZUMAB (T) IN HER2-POSITIVE (HER2+) EARLY BREAST CANCER (EBC): DATA FROM THE "REAL WORLD"

Oliva S.[1], Fini F.[2], Frattini S.[3], Simoncini E.[3], Pulignano G.[2], Giotta F.[1], Cioffi G.[4], Lestuzzi C.[5], Maurea N.[6], Rastelli F.[7], Gori S.[8]

[1]Cardiology Unit, NCI "Giovanni Paolo II", Bari; [2]Cardiology, S. Camillo Hospital, Roma; [3]Cardiology, Spedali Riuniti, Brescia; [4]Villa Bianca Hospital, Trento; [5]National Cancer Institute, Aviano; [6]National Cancer Institute, Napoli; [7]Oncology, Fermo; [8]Oncology, A.O. di Perugia

Background. Adjuvant trastuzumab improves DFS of HER2+ EBC pts. However, trastuzumab cardiotoxicity, as cardiac heart failure (CHF) or LVEF reduction, may appear in patients at increased cardiovascular risk.

Aims. To evaluate the relationship between ACEi/ARB and/or BB use and appearance of HF symptoms and/or changes in LVEF during adjuvant trastuzumab.

Patients and methods. Between January 2008 and June 2009, 253 HER2+EBC patients treated with adjuvant trastuzumab at 10 Italian institutions were retrospectively evaluated. They were divided in 4 subgroups according to the treatment with ACEi and/or BB: no BB-no ACEi/ARB; BB; ACEi/ARB; ACEi/ARB + BB. CHF symptoms and/or decrease in 10 points% of LVEF were recorded. LVEF was measured at baseline and 3-6-9-12 months after start of trastuzumab.

Results. CHF symptoms occurred in 2% of patients who did not take either ACEi/ARB or BB. CHF event-rate was increased in patients receiving one or both medications (partially justified by the increased cardiovascular risk). Prevalence of LVEF decrease >10 points% was similar in all subgroups. Trends in LVEF were characteristics for each study subgroup (Figure 1): at 3-month significant LVEF decrease was detected in ACEi/ARB and ACEi/ARB + BB group. Multiple logistic regression analysis showed that combined ACEi/ARB + BB therapy depended on hypertension history (OR 36.7, 95% 95% CI 4.3-315.5) and reduction of LVEF from baseline to 3-month evaluation (OR 0.88, 95% CI 0.78-0.97) (best prediction-3.5 points%, AUC 0.78, 95% 95% CI 0.65-0.91). No association was found between LVEF

changes and ACEi/ARB or BB therapy alone, which use was predicted for both medications only by hypertension history. LVEF recovery from 3- to 12-month was inversely related to the changes in LVEF from baseline to 3-month and trastuzumab restart was significantly higher in subgroup ACEi/ARB + BB although significant LVEF reduction in the first 3 months of therapy.

Conclusions. In clinical practice, hypertension history and changes in LVEF during the first 3 months of trastuzumab for EBC influence the use of ACEi/ARB and BB. LVEF recovery and the possibility to restart trastuzumab seem to suggest a protective effect of ACEi/ARB+BB.

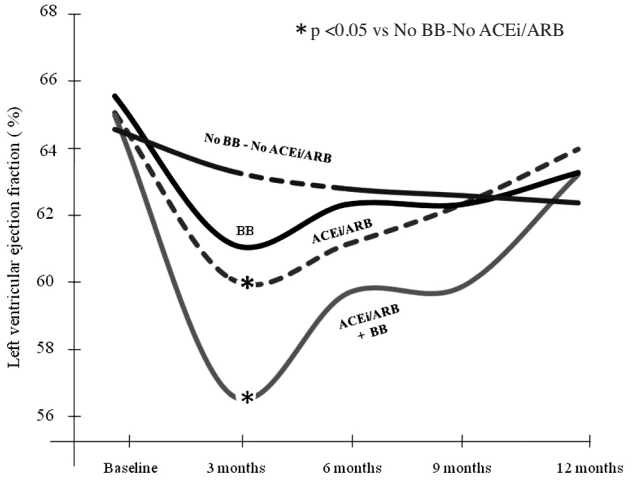


Figure 1 - LVEF according to 4 subgroups.

A39 ONCO-I2B2 PROJECT: A BIOINFORMATICS TOOL TO INTEGRATE BIOBANK OMICS-INFORMATION AND CLINICAL DATA TO SUPPORT TRANSLATIONAL RESEARCH IN ONCOLOGY

Segagni D.[a], Dagliati A.[c], Manera S.[a], Ronchetti E.[a], Tuscano A.[a], Villani L.[a], Pavesi L.[a], Bellazzi R.[b], Zambelli A.[a]

[a]IRCCS Fondazione S. Maugeri, Pavia, Italy; [b]Dipartimento di Informatica e Sistemistica, Università di Pavia, Italy; [c]Institute for Advanced Studies, Pavia, Italy

The ONCO-i2b2 project, supported by the University of Pavia and the Fondazione Salvatore Maugeri (FSM), aims at supporting translational research in oncology and exploits the software solutions implemented by the Informatics for Integrating Biology and the Bedside (i2b2) research center, an initiative funded by the NIH Roadmap National Centres for Biomedical Computing. The ONCO-i2b2 software is designed to integrate the i2b2 infrastructure with the FSM hospital information system and the institutional biobank, in order to provide well characterized cancer specimens along with an accurate patients clinical database.

The Breast Unit at FSM is the first one certified in Italy in accordance to the EUSOMA criteria. Each year, more than 600 of breast cancer patients come to the Breast Unit. The availability of the institutional biobank represents the core facility of breast cancer tissues, blood and primary cultures storage and collection for research purposes. More than 1000 specimens are currently stored and more than 200 of breast cancer patients give the consent for the use of specimens in the context of clinical research.

The i2b2 infrastructure provides a web-based access to all the electronic medical records of cancer patients, and allow researchers analyzing the vast amount of information, relying on a user-friendly interface. Data coming from multiple sources are integrated and jointly queried. During the integration process (Figure 1) the biological samples contained in a biobank are loaded into the i2b2 data warehouse through a series of Extract, Transform, Load operations.

In the future steps, we will empower the system implemented to far with a web-service that allows communication between i2b2 and the R statistical software. Relying on such module, we will develop a set of ONCO-i2b2 dedicated plug-in to perform further relevant analysis, with the goal of integrating patient's genotype data. Furthermore, using a genomic profiling approach, we will implement a pharmacogenomic-guided choice able to integrate clinical and "omics" data to provide optimal strategies of cure.

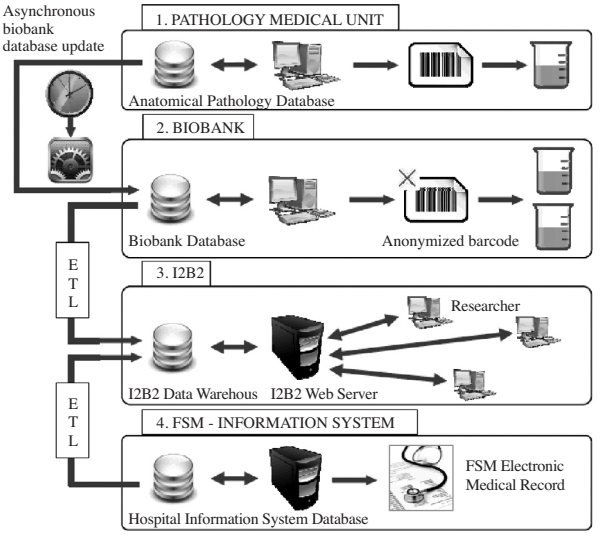


Figure 1 - ICT architecture designed to integrate information from the FSM medical units and the hospital information system.

A40 ASSOCIATION BETWEEN ULTRARAPID CYP2D6 POLYMORPHISMS AND ADVERSE DRUG REACTIONS AMONG WOMEN WITH BREAST CANCER TREATED WITH TAMOXIFEN

D'Agostino F.[1], Saggia C.[1], Forti L.[1], Rossi V.[1], Borra G.[1], Gaudino E.[1], Stratica F.[1], Rolla R.[2], Vidali M.[2], Bellomo G.[2], Alabiso O.[1, 2]

[1]S.C. Oncologia, AOU Maggiore della Carità, Novara; [2]Dipartimento di Scienze Mediche, Università del Piemonte Orientale Amedeo Avogadro, Novara

Background. Tamoxifen (TAM) has a key role in the management of women with hormone receptor (HR) positive breast cancer and requires enzymatic activation by CYP2D6 for the formation of active metabolites 4-hydroxytamoxifen and endoxifen. Retrospective clinical data suggests that polymorphisms of CYP2D6 can lead to null or reduced enzyme activity resulting in

worse outcomes for those individuals when treated with TAM. There is however a lack of robust prospective clinical data on this subject. In this study we evaluated whether CYP2D6 variation (Ultrarapid Metabolizer, UM) is associated with adverse reactions in women treated with TAM.

Methods. We analyzed 25 patients operated for HR breast cancer on adjuvant therapy with TAM for the presence of 16 genotype variants of CYP2D6 by INFINITI™ CYP2D6 assay, which utilizes AutoGenomics proprietary film-based microarray technology. All patients have been evaluated for adverse reactions and clinical outcomes.

Results. The prevalence of Extensive, Intermediate, Ultrarapid and Poor Metabolizers (EM, IM, UM, PM) was respectively 44% (11/25), 36% (9/25), 12% (3/25) and 8% (2/25), comparable with what has been previously reported in the Caucasian population.

TAM adverse reactions as hot flashes, endometrial thickening, headache, spotting, cramps and varices were present in all UM patients (3/3) but only in 2 out of 11 (18%) EM patients (difference statistically significant, $p = 0.027$). We considered EM arm as reference inasmuch is the commonest polymorphism in the study and general population.

Discussion. Based on these results a CYP2D6 genotyping before treatment to predict metabolizer status may open new avenues for individualizing endocrine treatment to avoid drug-related toxicities in the near future more than to prevent breast cancer recurrence. Furthermore it might be economically justified by potentially reducing adverse reactions in UM patients and hence cost management.

As the small number of patients and the short follow-up do not allow to reach any definitive conclusions, further examination is needed. The study is ongoing and we just enrolled 70 additional patients.

A41 PRESERVATION OF OVARIC FUNCTION AND PREGNANCY IN YOUNG EARLY BREAST CANCER (BC) SURVIVORS: SINGLE CENTER EXPERIENCE

Marcon I., Giardina G., Giaquinto A., Vallini I., Pinotti G.

Oncology Unit, Ospedale di Circolo, Varese

Background. BC accounts for one third of all neoplasms seen in reproductive-age women. Many of them have not yet got a family and consider getting pregnant. Adjuvant chemotherapy (CT) regimens used for the treatment can affect fertility and cause premature ovarian failure. Evidence from small studies has led to the use of LH-RHa to preserve fertility during CT but there is not conclusive data. Recent studies have shown that pregnancy following early BC is not detrimental on survival and seems to be protective.

Materials. Between 1999 and 2009 we identified 163 patients (pts) aged 40 or younger at diagnosis; median age at diagnosis was 35 (23-40). Physiological history, disease characteristics, treatment and its effect on fertility, incidence of sterility, desire of motherhood, number of pregnancies and outcome were evaluated.

Results. At a median follow-up of 61 months (range 4-182) 140 pts are alive; 110 pts were ER+ve. All pts were treated with CT, in 123 pts followed by endocrine therapy (LHRHa alone in 27 pts, tamoxifen in 21, LHRHa plus tamoxifen in 61, LHRHa plus AI in 14). Fifty pts received LHRHa during CT (for fertility preservation in 13 pts with ER-ve BC); eighty percent of them recovered regular menses. Ninety pts didn't receive LH-RHa: 52% maintained regular menses, 48% had amenorrhoea (permanent in 17%). Sixteen pregnancies were found in 13 pts: 8 completed, 5 hesitated in abortion (2 spontaneous and 3 volunteers); 2 pregnancies are ongoing and one pt was lost at follow-up. All newborns were healthy. One case of recurrent disease after pregnancy was found.

Conclusions. Pregnancy after BC is feasible and safe. Fertility counselling with multidisciplinary approach is highly recommended in young BC pts. There is no evidence that prior history of cancer increases the rates of malformations in newborns.

A42 DIAGNOSIS OF BREAST CANCER METASTASES WITH PET/TC IN PATIENTS WITH ELEVATION OF TUMOUR MARKERS: FIRST DATA UPDATE

Mafodda A., Prestifilippo A., Aricò D.*, Vadalà A.*, Mare M., Fornito C.*, Giuffrida D.

*Istituto Oncologico del Mediterraneo, Viagrande, Catania, Italy; *ARNAS Garibaldi Nesima, Catania, Italy*

Background. Breast cancer is one of the most common cancers worldwide. PET/CT is more accurate than traditional methods for the detection of distant metastases or local recurrence and enables for early assessment of treatment response in patients after surgery for breast cancer undergoing primary chemotherapy. PET/CT is not considered a conventional examination during follow-up of patients with breast cancer, but recent data indicate its usefulness both in cases of asymptomatic increase of tumour markers and in uncertain conventional imaging results. This study investigates the potential role of PET/CT to detect clinically occult metastases in patients with suspected recurrence of breast cancer during follow-up.

Methods. The authors studied 51 patients in breast cancer follow-up after primary surgery and chemotherapy and/or external radiotherapy. All patients were in remission without any other clinical or instrumental signs of relapses, except for the progressive elevation of CA 15.3 and/or CEA, tested during the follow-up. In 44 patients conventional imaging provided uncertain results and increase of CA 15.3 that was not correlated to any evidence of metastatic disease.

Results. Disease relapse was proven in 48 out of 51 patients and successfully PET/CT has identified clinically occult disease with an excellent sensitivity. In 21 cases the anatomical distribution of metastasis sites was in the bone, 11 in the lymph node, 7 in the lung and 9 in the liver. Out of them we found 2 false-negative and 1 false-positive.

Conclusions. PET/TC may be more sensitive than the serum tumour markers in detecting relapse of breast cancer. This study demonstrated the clinical utility of tumour marker-guided PET in the follow-up of breast cancer patients.

A43 THE ANTI-NEOPLASTIC ERBB2-ANTIBODY 2C4 PRODUCES LEFT VENTRICULAR DYSFUNCTION IN MURINE HEARTS

Coppola C.[1], Tocchetti C.G.[1], Barbieri A.[1], Rea D.[1], Fedele C.[2], Malara E.[2], Arra C.[1], D'Alessio G.[2], Iaffaioli R.V.[1], De Lorenzo C.[2], Maurea N.[1]

[1]National Cancer Institute, Sen. Pascale Foundation, Naples; [2]Federico II University, Naples, Italy

Purpose. Anti-ErbB2 therapies have greatly improved the prognosis of patients with breast cancer. Unfortunately, such treatments are associated with an increased risk of left ventricular (LV) dysfunction. Trastuzumab (Herceptin), the prototypical ErbB-targeted therapy, increases the frequency of asymptomatic decrease in LV ejection fraction (LVEF) by 3-18%, and the risk of heart failure (HF) by 2-4%. The newer ErbB2 antibody rhuMAb 2C4 (pertuzumab) seems to affect ligand induced ErbB signaling in a more direct fashion, affecting EGFR/ErbB2 dimerization; yet, its cardiac side effects are only beginning to emerge. Here, we test whether the murine 2C4 induces cardiac dysfunction in normal mice.

Methods. *In vivo* cardiac function was measured with LV fractional shortening (FS) by M-mode echocardiography in sedated C57BL/6 mice (2-4 mos old) at day 0, and after 2 and 6 days of daily i.p. administration of 2C4 (2.25 μg/g/day) or doxorubicin (Doxo, 2.17 μg/g/day) as a positive control, and in sham animals. With Speckle Tracking echocardiography (ST) we also evaluated radial myocardial strain (%), a very sensitive parameter which can predict LV dysfunction.

Results. After only 2 days of treatment, FS was reduced with 2C4: 58 ± 1%, p = .01 vs sham (60 ± 0.4%). The reduction in FS obtained with Doxo was even larger: 52 ± 0.2%, p = .0000001 vs sham, p = .00004 vs 2C4. Myocardial strain was similarly reduced in both 2C4 (40 ± 8%) and Doxo-treated mice (43 ± 3%) compared to sham (66 ± 0.6%; p = .02 vs 2C4, and p = .0005 vs Doxo). After 6 days of treatment, LV dysfunction was exacerbated, with FS further reduced to similar values by 2C4 (39 ± 5%) and Doxo (46 ± 2%, p = NS vs 2C4; both p <.05 vs sham and vs 2 days), and strain decreased to 31 ± 7% (2C4) and 40 ± 7% (Doxo, p = NS vs 2C4; both p = .01 vs sham and p = NS vs 2 days).

Conclusions. The murine ErbB2 antibody 2C4 is cardiotoxic in mice. The reduction in FS is milder than Doxo early at 2 days, but comparable to Doxo after 6 days. The clear mechanisms of anti ErbB2 therapies-induced cardiotoxicity are to be elucidated. Further studies will be crucial to establish the cardiotoxic mechanisms of ErbB2-antagonists, and to influence the design of future anticancer therapies in an attempt to retain anticancer effects, while minimizing cardiac toxicity. We also plan to apply speckle tracking echocardiography to clinical studies, in order to evaluate the impact of early identification of ErbB2-blockers cardiotoxicity in the treatment of women with breast cancer.

A44 HER2 FLUORESCENT *IN SITU* HYBRIDIZATION (FISH) GENE AMPLIFICATION CONCORDANCE BETWEEN PRIMITIVE NEOPLASM AND METASTASIS IN BREAST CANCER

Rossi V., Saggia C., D'Agostino F., Bertona E., Gaudino E., Forti L., Negru M.E., Rigon E., Genestroni S., Sponghini A.P., Rondonotti D., Ritorna A., Alabiso O.

S.C. Oncologia Medica, AOU Maggiore della Carità, Novara

Background. HER2 is a well-known oncogene used as both a prognostic and predictive marker for breast cancer. Usually Her2 assessment is exclusively performed on the primary tumour, assuming that it is also representative of metastatic lesions.

However literature suggests that metastatic and primary tumours may vary in terms of HER2 expression. This difference may be caused by intratumoral heterogeneity, real tumoral biological change or technical and interpretational variabilities in laboratory data.

In this study we evaluated our casuistry to better understand if metastatic lesions' reassessment of HER2 status can be useful in clinical practice.

Methods. Twenty patients with HER2-positive primary breast cancer and paired metastasis were evaluated. HER2 status was determined by FISH because of suboptimal reproducibility of other measurement methods.

Results. At first evaluation 15 patients (75%) had HER2 status agreement between paired tumours; in the discordant tumour pairs (5 patients, 25%) FISH analysis has been repeated and the agreement was therefore reached in 16 patients (80%).

One of 4 discordant tumour pairs presented HER2 negative primary tumour and HER2 positive lung metastasis: we evaluated again the primary neoplasm and found out rare HER2 amplified cells. So we supposed a clonal selection during metastatic process resulting from original intratumoral heterogeneity.

Two patients (10%) had primary tumour HER2 negative and secondary tumours HER2 positive. At last 1 patient had primary tumour HER2 positive and secondary tumour negative.

Discussion. A fair amount of breast cancer changes HER2 status in the disease's course and this is probably linked to genetic instability of tumoral cells during the metastatic process and could be favored by antineoplastic agents' use.

In conclusion this study suggests that metastatic tumours can have a different profile than the primary, and that HER2 reassessment in metastatic lesions should take place and may lead to different treatments.

A45 PROGNOSTIC POTENTIAL OF KI 67 IN EARLY BREAST CANCER: A RETROSPECTIVE ANALYSIS OF 1672 PATIENTS IN A SINGLE INSTITUTION EXPERIENCE

Visintin R., Gambini D., Consonni D.*, Locatelli E., Galassi B., Bareggi C., Runza L.§, Giroda M.^, Tomirotti M.

*U.O. Oncologia Medica, *U.O. Epidemiologia, §Unità di Anatomia Patologica, ^U.O. Chirurgia Generale I/Plastica Senologica, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milano*

Ki 67 antigen is used to evaluate the proliferative activity in breast cancer. Despite the large number of published papers, most of them retrospective, its role as a prognostic marker is still undefined.

In order to verify its prognostic potential in a homogeneous setting, we performed a retrospective analysis of our breast cancer patients' data, collected since 1995 in a prospectically oriented database.

Ki 67 value was defined as low (≤10%), intermediate (11-20%), and high (>20%).

For the three levels of Ki 67 we calculated Hazard Ratios (HR) and 95% confidence intervals (95% CI) univariate and multiple Cox models.

As of April 2011, we found 1672 early breast cancer patients with Ki 67 levels. Despite a negative impact of high Ki 67 on disease-free survival (DFS) [crude HR 2.07 (95% CI 1.38-3.12); p <0.001], this association disappeared when we adjusted for age

at diagnosis, stage, estrogen receptors and HER-2 status, and treatment [HR 1.10 (95% CI 0.69-1.75); p = 0.69]. We confirmed the strong independent prognostic importance of all the other clinical covariates included in the multiple Cox regression model, except for HER-2 status.

Conclusions. In a retrospective analysis of a large homogeneous sample of breast cancer patients, Ki 67 levels were not associated with DFS when we adjusted for other known strong prognostic factors (age, stage, estrogen receptors, and therapy).

A46 PROGNOSTIC AND PREDICTIVE ROLE OF CIRCULATING ENDOTHELIAL PROGENITOR CELLS IN BREAST CANCER PATIENTS

Fotia V., Zambelli A., Della Porta M.G., Rosti V., Galizzi G., Amato A., Eterno V., Pagani A., Pavesi L., Riccardi A.

IRCCS, Fondazione S. Maugeri, Pavia

Background. Cancer is largely dependent on tumour neoangiogenesis, with evidence of vascular endothelial dysfunction. Novel ways to assess vascular function in cancer include measuring levels of circulating endothelial cells (CEC). An additional circulating cell population are endothelial progenitor cells (EPC), which have the ability to form endothelial colonies *in vitro* and may contribute toward vasculogenesis. At present, there is great interest in evaluating the role of EPC as novel markers for tumour angiogenesis and drug therapy monitoring.

Aim. To investigate the role of EPC in prediction of treatment-response and prognosis in metastatic (mBC) and early breast cancer (eBC).

Patients and methods. From February 2010 to February 2011, 12 eBC and 12 mBC, receiving chemotherapy consisting of anthracyclines-based and taxanes-based (± bevacizumab) treatment respectively, entered the protocol and were analyzed for EPC levels. EPC were evaluated with both a functional clonogenic assay (quantification of EPC-colony forming unit) and morphologic cytofluorimetric analysis (CD133+/ VEGFR2+/CD34+ and CD45-) at different time-points (before surgery and/or treatment, end of treatment and in case of PD).

Results. After a median follow-up of 8 months 4/12 mBC patients obtained PR and 2 patients had SD. The remaining 6 patients showed PD under treatment. As compare to baseline data, 3/4 responders manifested a decrease in the number of EPC, while 5/6 pts in PD had an increase number of EPC, evaluated according to morphologic and functional assays.

As for eBC, the baseline EPC enumeration was higher in patients with large tumour burden (pT3/4, 2/12) as compare to patients with less extensive disease (pT1/2, 10/12), suggesting a possible correlation with tumour staging.

Conclusion. Taken together these early data generate the hypothesis of possible predictive role of EPC in treatment monitoring in mBC setting and suggest that EPC enumeration can be investigated as possible prognostic marker in eBC. Further analyses are needed to confirm these preliminary results.

A47 NEOADJUVANT THERAPY WITH PACLITAXEL FOLLOWED BY ANTHRACYCLINE-BASED REGIMEN AND CONCURRENT TRASTUZUMAB IN HER2-POSITIVE (HER2+) BREAST CANCER (BC)

Fabbri M.A.[1], Foglietta J.[3], Moscetti L.[1], Anastasi P.[3], Massari A.[2], Ruggeri E.M.[1], D'Auria G.[1], Basurto C.[3], Stocchi L.[3], Gori S.[3]

[1]Medical Oncology, [2]Pathology, C.O. Belcolle, AUSL Viterbo; [3]Medical Oncology, S. Maria della Misericordia Hospital, Perugia

Background. Neoadjuvant treatment with anthracycline-based therapy and concurrent trastuzumab demonstrated a pCR rate of 65% in HER2+ BC without clinical congestive heart failure (CHF) (JCO 2005; 23: 3676-85).

Methods. Between 02/2006 and 09/2010, 23 patients with histologically confirmed stage II to III invasive HER2+ BC not candidates for conservative surgery were treated with neoadjuvant regimen: paclitaxel 80 mg/m^2/weekly for 12 weeks followed by FEC (epirubicin 75 mg/m^2) for 4 cycles given concurrently with trastuzumab 2 mg/kg/weekly (loading dose 4 mg/kg) for 24 weeks. After surgery, trastuzumab was given to complete 1 year of trastuzumab treatment.

Tumour response was assessed by mammogram and ultrasound at baseline, after paclitaxel + trastuzumab and before surgery. pCR was defined as no invasive tumour both in breast and axilla. Cardiac evaluation by electrocardiogram and echocardiography was performed at baseline, after completation of paclitaxel + trastuzumab, before surgery and then every 3 months during adjuvant trastuzumab treatment.

Results. Five pts had clinical stage IIA, 8 IIB, 6 IIIA, 2 IIIB and 2 IIIC; median age was 49 years (27-68); clinical axillary node involvement was detected in 17 pts and HR-positivity in 13; Ki-67 value was ≥30% in 17. We reported pCR in 12 pts (52%), pPR in 9 (39%) and SD in 2 (9%). Two out of 9 pts with pPR obtained a pCR only in breast.

Conservative surgery was performed in 7 pts (30%). Adjuvant trastuzumab was administered to 13 pts, while 10 pts are still ongoing. Reduction of LEVF >10% was observed in 2 pts. One patient developed G3 CHF (LEVF value of 34%) after the third cycle of FEC. Chemotherapy was stopped and the pt underwent surgery and adjuvant trastuzumab. This patient died 3 months after the end of trastuzumab due to tapazol febrile neutropenia. No other unexpected grade 3/4 toxicities were observed.

Conclusion. Neoadjuvant therapy with paclitaxel followed by anthracycline-based regimen and concurrent trastuzumab in HER2+ BC showed high rates of pCR with acceptable cardiac toxicity.

A48 GENETIC POLYMORPHISMS AND ASSESSMENT OF NEUTROPENIA AFTER DOCETAXEL CHEMOTHERAPY IN BREAST CANCER

Pellegrini P., De Iuliis F., Russo I., Di Trapani M.C., Gentile G., Simmaco M., Roselli A., Trasatti L., Marchetti P.

Sant'Andrea Hospital, University of Rome "La Sapienza", Italy

Background. Chemotherapy-induced neutropenia is a major risk factor for infection-related morbidity and mortality and also a significant dose-limiting toxicity in cancer treatment. Taxanes

are the most active agents in the treatment of breast cancer. Evidence from randomised controlled trials suggests that the incidence of FN (febrile neutropenia) in patients affected by breast cancer in treatment with docetaxel is around 15%. To understand why only some patients experience severe neutropenia the metabolic pathways of this drug have to be unraveled in detail. The aim of our study was to evaluate the association between docetaxel-neutropenia and genetic polymorphisms related to its metabolism.

Materials and methods. We studied 100 patients (age 53.3 ± 8.5 DS) affected by breast cancer and under treatment with docetaxel; we genotyped them for selected polymorphisms and ABC-transporters that may influence cellular sensitivity to taxanes: CYP3A4* 1B (A >G), CYP3A5* 3 (G >A) and ABCB1 (1236 C >T; 3435 C >T). SNPs (Single Nucleotide Polymorphism) were carachterized by pyrosequencing. The statistical survey was conducted by SPSS 14.2 software.

Results. For patients homozygous for CYP3A4* 1B and CYP3A5* 3 although without statistical significance ($p > 0.005$) we can demonstrate a greatest incidence of grade 3/4 neutropenia after the first course of docetaxel. Patients homozygous for ABCB1 polymorphisms have a lower haematological toxicity after therapy with docetaxel.

Conclusions. We suggest that CYP3A4, CYP3A5 and ABCB1 might affect taxane haematological toxicity. In the future, studies with SNP chips should be performed in order to identify signatures differentiating between patients with high or lower risk of neutropenia linked to docetaxel chemotherapy. Genetic polymorphisms should suggest or not the use of G-CSF primary prophylaxis.

A49 TIME-2-CHANGE: RETROSPECTIVE, MULTICENTER, OBSERVATIONAL STUDY OF THE CLINICAL USE OF ADJUVANT HORMONAL THERAPIES FOR BREAST CANCER (BC) PATIENTS IN TWO TIME PERIODS IN THE LIGHT OF RECENT CHANGES IN NATIONAL AND INTERNATIONAL GUIDELINES

Fiorio E.[1], Parolin V.[1], Spazzapan S.[2], Frisinghelli M.[3], Crivellari D.[2], Galligioni E.[3], Spada A.[2], Molino A.[1]

[1]Oncologia Medica, AOUI Verona; [2]Oncologia Medica C, CRO di Aviano, Pordenone; [3]Oncologia, Ospedale Santa Chiara, Trento

Introduction. Since 2006, national and international guidelines have recommended the use of aromatase inhibitors (AIs) in postmenopausal women with hormone-sensitive EBC (early breast cancer). The currently available strategies are five years' use after surgery or after 2-3 years of tamoxifen (T). The primary aim of this study was to compare the frequency of first adjuvant hormonal treatment (HT) with T or AIs in the 12 months of 2006 and 2008. The secondary aims were to compare the frequencies of the two strategies, the type of second hormonal treatment, and the types of adverse events (AEs).

Materials and methods. We retrospectively reviewed the data (pathological stage, histological type, receptor and HER-2 status, locoregional treatment, adjuvant HT, treatment-related events, and the recurrence of BC) of 500 postmenopausal EBC patients treated in Verona (265), Aviano (206) and Trento (29), 243 of whom started adjuvant HT between January and December 2006, and 257 between January and December 2008.

Results. Between January and December 2006, 54% started adjuvant HT with AI, 44% started T and 2% started combined therapy (T + IA); the corresponding figures between January and December 2008 were 75%, 23% and 2%. There was a 21% increase in the post-surgical use of AIs between the two periods (from 40% to 54% in Aviano [$p = 0.04$], and from 68% to 90% in Verona [$p < 0.0001$]), with less use of anastrozole (from 51% to 31%) and more use of letrozole (from 5% to 44%). The most frequently prescribed regimen in both periods was upfront. The initial HT was changed because of adverse events or disease recurrence or progression in 14% in 2006 and 8% in 2008, with AEs accounting for the changes in 5% in 2006 and 4% in 2008.

Conclusions. The factors influencing the prescription of IAs as adjuvant HT were risk category, the time of initial treatment (2006 vs 2008) and center, which suggests that clinical practice was influenced by national and international recommendations.

Study supported by Astrazeneca.

A50 DIFFERENT OUTCOME OF BONE METASTATIC BREAST CANCER PATIENTS ACCORDING TO CLINICAL FEATURES

Ricevuto E.[1], Irelli A.[1], Cannita K.[1], Bruera G.[1], Adinolfi I.[1], Cocciolone V.[1], Brollo M.[1], Palluzzi E.[1], Sarno I.[1], Rinaldi L.[1], Rucci N.[2], Teti A.[2], Ficorella C.[1]

[1]Medical Oncology, "S. Salvatore" Hospital, [2]Department of Experimental Medicine, University of L'Aquila

Between 1993 and 2010, 127 women harbouring bone metastases from breast cancer (BC) were followed at Medical Oncology, San Salvatore Hospital, University of L'Aquila. Features of bone metastases: multiple bone sites 113 (89%), one bone site 14 (11%); osteolytic lesions 89 (70%), osteosclerotic lesions 13 (10%), mixed lesions 16 (13%), undetermined 9 (7%). Involved sites: spinal column, 105 (83%); pelvis/hip, 84 (66%); long bones, 58 (46%); other skeletal sites, 104 (82%). Bone metastases: metachronous 101 (80%); synchronous 26 (20%). Dynamic evaluation over time of BC patients (pts) showed the following distribution of bone metastases at median follow-up of 81 months: bone-only, 45 patients (35.4%) (group 1), bone and visceral metastatic, 82 pts (64.6%). Among bone and visceral metastatic (M) BC pts: bone and metachronous visceral, 43 patients (33.9%) (group 2); synchronous bone and visceral, 23 patients (18.1%) (group 3); visceral and metachronous bone, 16 patients (12.6%) (group 4). Overall median disease-free survival (DFS) of BC pts who developed bone metastases was 36 months; median time to detection of bone metastases from diagnosis was 42 months; median overall survival (OS) was 88 months. Comparison of DFS and OS (Log Rank test) among BC pts who developed bone metastases and remained bone-only (group 1) or developed visceral metastases (group 2) was statistically significant ($p = 0.049$ and $p = 0.010$, respectively) with median DFS of 37 and 34 months, respectively, and median OS of 120 and 86 months respectively. Median OS of bone MBC pts was 28 months. Comparison of OS (Log Rank test) of bone metastatic disease among group 1 and group 2 was not statistically significant ($p = 0.592$) with median OS of 30 and 39 months, respectively. Present data show that clinical outcome of BC pts who primarily develop bone metastases is significantly different between pts who maintain bone-limited metastatic BC or develop visceral metastases. Further assessments of groups 1 and 2 are currently underway with the aim of better characterizing bone metastatic disease.

A51 LIPOFILLING IN BREAST CANCER PATIENTS: A PLASTIC SURGERY TECHNIQUE OR A STEM CELLS BASED THERAPY?

Eterno V.[1], Petrolo G.[3], Zanini V.[3], Villani L.[4], Zambelli A.[1,2], Pavesi L.[1,2], Amato A.[1]

[1]Laboratory of Experimental Oncology and Pharmacogenomics, [2]Unit of Medical Oncology, [3]Unit of Senology, [4]Unit of Pathology, IRCCS Salvatore Maugeri Foundation, Pavia

Mesenchymal stem cells are undifferentiated cells with the potential to differentiate into several cell types, even of different embryonic origin. They display a crucial role in regeneration of damaged tissues and show an extraordinary proangiogenic potential. Adipose tissue is a reservoir of ASCs dispersed in the stromal fraction of lipoaspirates. They are abundant and easy to obtain with minimal discomfort of the patient. Those features make them a good candidate for cell based-therapy.

In the last years at the Breast Unit of S. Maugeri Foundation in Pavia, lipoaspirates have been used for autologous implantation in mammary tissues promoting maintenance of shape and volume of breast in patient undergoing conservative breast surgery, moreover it was found a great improving in vascularization and global health of the breast tissues.

Indeed, ASCs have been proposed to stabilize autologous fat grafts for regenerative therapy, however the lack of comprehensive view of the molecular pathways governing their biological properties remains a primary obstacle to their safety in clinical application.

In this study, we set a protocol for isolation and characterization of ASCs derived from 20 lipoaspirates of human donors, undergoing lipofilling for breast modelling after cancer resection, to better understand the interaction mechanisms occurring between ASCs and breast cancer cells and to avoid side effects of ASCs implantation.

Here we found that 5 mL of lipoaspirates generate a great amount of ASCs in cell culture. We showed that those cells are of mesenchymal origin since they express vimentin, a well known mesenchymal marker and they are not hematopoietic since they do not express CD45. Moreover, we found that they display several features of stem cells: anchorage-independent growth, differentiation potential as adipogenic, chondrogenic, osteogenic and myogenic lineage, and expression of surface markers as CD133, CD44, CD90 and CD70, recognized to be expressed in undifferentiated/multipotent cells. The implementation of biological and molecular characterization of ASCs could contribute to better understand the safety and efficacy of lipofilling procedures in breast cancer patients.

A52 NEUTROPENIA WITH ADJUVANT EPIRUBICIN-CMF CONFERS IMPROVED SURVIVAL IN PATIENTS WITH NODE-NEGATIVE OR 1-3 NODE-POSITIVE RAPIDLY PROLIFERATING BREAST CANCER

Kopf B., Scarpi E., Casadei Giunchi D., Faedi M., Gianni L., Rocca A., Zoli W., Silvestrini R., Amadori D., De Giorgi U.

Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), Meldola (FC)

Background. Patients who experience at least some degree of neutropenia while on their adjuvant chemotherapy for breast cancer may have an improved survival. Tumour proliferation is a prognostic marker in breast cancer. We therefore additionally hypothesized that patients with rapidly proliferating breast cancer and evidence of neutropenia while on adjuvant chemotherapy would have a better survival than similar patients for whom there was no evidence of myelotoxicity.

Methods. We therefore reviewed the case notes of 173 women treated at the Area Vasta Romagna cancer centers with epirubicin, followed by intravenous CMF (cyclophosphamide, methotrexate and 5-fluorouracil) regimen or the inverse sequence for rapidly proliferating breast cancer, as defined by thymidine labeling index >3%, to identify patient- and treatment-related factors influencing outcome.

Results. The actuarial 5-year overall survival for these women was 94%, with the anticipated poorer outcome for those with higher proliferation index (≥10% vs 3-10%, $p = 0.032$). There was no evidence that estrogen receptor-negative tumours, HER-2 positive disease or older age at presentation resulted in a poorer survival. Of particular interest was the observation that the absolute survival advantage resulted confined in the 47% of patients who had grade 3-4 neutropenia ($p < 0.001$) over those with grade 0-2 neutropenia ($p = 0.268$).

Conclusion. Our results strongly suggest that neutropenia has more influence on outcome than age and tumour biological factors in patients with rapidly proliferating breast cancer.

A53 NEOADJUVANT TREATMENT WITH TRASTUZUMAB IN HER2-POSITIVE BREAST CANCER: PIVOTAL STUDY

Mentuccia L.[1], Magnolfi E.[1], Iafrate G.[2], Vaccaro A.[1], Giagu S.[3], Ramieri M.T.[4], Sperduti I.[1], Iorio C.[3], Marigliani M.[2], Gamucci T.[1]

[1]Medical Oncology Unit, Sora (Frosinone); [2]Department of Surgery, Sora (Frosinone); [3]Department of Radiology, Sora (Frosinone); [4]Department of Pathology, Frosinone

Background. In women with HER2+ locally advanced breast cancer (BC), the addition of trastuzumab (T) to chemotherapy (CT) before surgery increases the rate of pathological complete response (pCR); the necessity of concurrent administration of T with an anthracyclines-containing CT has already been called into question by L. Del Mastro (Ann Oncol, June 2010). We report our experience in support of this hypothesis: we conducted a pivotal study to evaluate the activity of a neoadjuvant CT regimen in which T is given with a taxane but not with the anthracyclines in women with HER2+ locally advanced BC.

Methods. Starting from 2006 until today we treated 17 patients (pts) with histologically invasive HER2+ (3+ or FISH+) BC not suitable for conservative surgery with the CT regimen: epirubicin/cyclophosphamide (EC) (100/600 mg/m^2) q3w for 4 cycles followed by 4 cycles docetaxel (D) (100 mg/m^2) with prophylactic G-CSF given concurrently with T 2 mg/kg/w (loading dose: 4 mg/kg). pCR was defined as no invasive tumour residuals in breast and nodes. T was continued after surgery for a total of 52 weeks. Cardiac evaluation included an echocardiogram performed at baseline, after four cycles EC, at the end of CT and every 3 months.

Results. Median age at diagnosis 47 (range 32-72); premenopausal 64.7%; Ki 67 >15% 88.2%; G2 35.3%, G3 64.7%; stage III 58.8%, stage II 41.2%; ER+/PgR+ 64.7%.

Thirteen pts are evaluable for response; conservative surgery was performed in 7 pts (53.8%).

Eight pts (61.5%, 95% CI 31.5-88) achieved pCR and 4 pts pPR with pT <1cm and pN0; at a median follow-up of 24 months (range 9-80) all are alive without disease. One patient didn't respond to CT and died with recurrent disease at 3 years.

Conclusions. The neoadjuvant CT with EC for 4 cycles followed by four cycles D given concurrently with T leads to a good rate of response without cardiac events. Data collection is ongoing and update results will be presented.

A54 IMPROVED HEALTH PERCEPTION DUE TO GENETIC COUNSELING FOR WOMEN FREE OF DISEASE ATTENDING A HIGH RISK CLINIC FOR BREAST AND/OR OVARIAN CANCER

Catania C., Feroce I., Barile M., Goldhirsch A., De Pas T., de Braud F., Boselli S., Adamoli L., Radice D., Rossi A., Bonanni B.

European Institute of Oncology, Milan

Background. Subjects referred to genetic counseling for family or personal history of breast and/or ovarian cancer discuss with the genetic counselor and the physician their cancer risk, the probability of germinal mutations in the family, the advantages, limitations and clinical implications of performing genetic test. Usually, individuals referred to genetic counseling have a somewhat peculiar perception of illness and death even if healthy and feel a strong sense of responsibility towards relatives. We investigated these aspects pre/post counseling in high-risk healthy women and in patients after breast or ovarian cancer diagnosis, but free of disease.

Methods. To assess changes in fears of illness and death and cancer risk perceptions after counseling and test, three different questionnaires were submitted: before counseling, within 20 days and after genetic test.

Results. We evaluated 151 subjects. Before counseling 89% were worried about their risk of disease; 58% felt "different" because of their personal and familial history; 40% were influenced in their life choices by cancer fear. After counseling 82% of the subjects felt better about their pre-existing fears, the interview allowed 53% to clarify the meaning of disease risk, positively influencing their life choices. All subjects but one decided to perform genetic test; at the time of writing 97 were available and 33 (33%) were positive. The knowledge of positivity increased fears in 29/33 (88%). All 33 subjects felt safer (85%: much/very much) in being followed by a dedicated staff. Fifty-two (52%) subjects had an uninformative test (wild type), 85% of them were not worried by uncertainty and 94% considered counseling very useful anyway.

Conclusions. Candidates to genetic counseling have frequently an increased perception of being ill, which influences their ability to make decisions during life. Genetic counseling often improves this perception in disease-free subjects and facilitates life plans. After testing (positive and negative) most women feel satisfied and much safer for being properly followed by a professionally and humanly qualified staff.

A55 THE IMPACT OF PREOPERATIVE BREAST MAGNETIC RESONANCE IMAGING ON SURGICAL TREATMENT IN WOMEN WITH BREAST CANCER IN PROVINCE OF MODENA

De Matteis E., Cortesi L., Cirilli C., Sebastiani F., Federico M.

Department of Oncology and Hematology and Disease of the Respiratory System, University of Modena and Reggio Emilia, Italy

Aims and background. The use of preoperative breast magnetic resonance imaging (MRI) has increased recently to determine the surgical management for early and advanced breast cancer. This study aims to evaluate the frequency of breast MRI utilization over the years and its impact on surgical treatment. The secondary objective is to compare the prognosis between patients undergoing preoperative breast MRI and patients not referred to this examination.

Methods. Study population was retrieved from the Modena Cancer Registry (RTM) database concerning 2213 women residents in the province of Modena diagnosed with locally advanced or large operable breast cancer between 2004 and 2007. We evaluated difference between patients treated with neoadjuvant chemoteraphy (NACT) who performed preoperative MRI (MRI-group) and patients who did not perform the examination (no MRI-group), on surgery treatment and outcome.

Results. From 2004 to 2009, a total of 296 women have received NACT. Among these women, we recognized 81 patients belonging to MRI-group. Of MRI-group, 36 (44.4%) underwent BCS and 45 (55.6%) mastectomy. Among no MRI-group (n = 149), 71 (47.7%) underwent BCS and 78 (52.3%) mastectomy. After a median follow-up period of 5 years, the OS appears to be 81% for the MRI group and 78% for the no MRI group (p = NS). The DFS at 5 years was 72% for the first group, and 71% for the second group (p = NS).

Conclusions. Our results compare favourably with those of literature and suggest that preoperative MRI does not reduce the number of mastectomies. In fact there isn't a statistically significant difference in terms of surgery among women who performed MRI and those that have not performed the examination. In addition, there is no difference between the two groups in terms of OS and DFS.

A56 IMPACT OF TRASTUZUMAB (T)-BASED THERAPY ON CLINICAL OUTCOME IN PATIENTS WITH HER-2 POSITIVE EARLY BREAST CANCER (EBC): UPDATE OF A SOUTHERN ITALY MULTICENTER, OBSERVATIONAL STUDY

Adamo V.[1], Ricciardi G.R.R.[1], Adamo B.[1], Agostara B.[2], Caruso M.[3], Gebbia V.[4], Gebbia N.[5], Lavenia G.[6], Banna G.L.[7], Mafodda A.[8], Rossello R.[1], Butera A.[9], Spada S.[10], Borsellino N.[11], Mangiameli A.[12], Campiglio M.[13], Tuccari G.[1] on behalf of AIOM-SIAPEC Sicilian group

[1]Department of Human Pathology, Unit Integrated Therapies in Oncology, University of Messina; [2]Medical Oncology, Hospital M. Ascoli, Palermo; [3]Humanitas Centro Catanese di Oncologia, Catania; [4]La Maddalena Clinic for Cancer, University of Palermo; [5]Medical Oncology Policlinic "P. Giaccone", Palermo; [6]Medical Oncology Hospital, Catania; [7]Division of Medical On-

cology, Cannizzaro Hospital, Catania; [8]Mediterranean Institute of Oncology Viagrande, Catania; [9]Medical Oncology Hospital, Agrigento; [10]Medical Oncology Hospital, Siracusa; [11]Medical Oncology Unit, Buccheri La Ferla Fatebenefratelli Hospital, Palermo; [12]Medical Oncology, Hospital Musumeci, Catania; [13]Fondazione IRCCS, Istituto Nazionale Tumori, Milan

Background. cErb-B2 (HER-2) has shown to be over-expressed in 20-25% of primary breast cancer, and is associated with poor prognosis. Some large, randomized studies have reported a significant reduction in the risk of recurrence when trastuzumab is administered with chemotherapy in EBC HER2+ cancer.

Methods. This observational, multicenter, retrospective study was conducted in 12 oncology centers in Sicily during 2006-2010. Inclusion criteria: age ≥18 years, surgery for early breast cancer, diagnosis of invasive disease, HER-2 positivity as defined by current guidelines and treatment with T.

Results. 569 patients (pts) were included. Surgical outcomes: quadrantectomy 58.1%, mastectomy 33.7% and tumorectomy 8.2%. Tumour stage: T1 50.6%, T2 37.9% and T3 11.5%. Histology: invasive ductal carcinoma 94.7%. Histological Grade: G3 55.6%. Node status: N0 52.6%, N1 27.3%, N2 12.5%, N3 6.7% and Nx 0.9%. Hormonal status: estrogen receptor positive 60.1% and progesterone receptor positive 47.3%. Proliferation: Ki67 ≥10% in 82.4%. Neoadjuvant and adjuvant T was administered in 11.9% and 93.4% pts, respectively. Sequential administration of T after adjuvant chemotherapy was the most common schedule. Cytotoxic agents used: anthracyclines 76.04%, taxanes 33.02% and both agents in combination 26.8%. Relapses were observed in 5.6% patients. The main metastatic sites were: liver 18.75%, bone 12.5%, lung 12.75%, brain 12.75%, locoregional and contralateral 12% and lymph nodes 9.4%. N positivity and hormone receptor negativity are significantly associated to relapse. Cardiac toxicity (LVEF reduction >10%) was observed in 3.5% pts. DFS at 25 months of FU was similar to that of HERA DFS at 23.5 months of FU.

Conclusions. Our study confirms the efficacy and safety of T in early HER2+ breast cancer, although includes a better prognostic population. These data indicate a satisfactory level of adherence to the international guidelines in the management in HER-2 positive EBC either in term of expression of cErb-B2 either in terms of treatment, showing a significant improvement in DFS when trastuzumab was added to adjuvant chemotherapy.

A57 USE IN CURRENT CLINICAL PRACTICE OF 70-GENE SIGNATURE IN EARLY BREAST CANCER

Bighin C.[1], Del Mastro L.[1], Canavese G.[2], Carli F.[3], Levaggi A.[1], Giraudi S.[1], Lambertini M.[1], Iacono G.[1], Pronzato P.[1]

[1]S.C. Oncologia Medica A, [2]S.S. Senologia Chirurgica, [3]S.C. Anatomia Patologica, Istituto Nazionale per la Ricerca sul Cancro, Genova

One of the aims of gene expression profiling is to identify early breast cancer patients with a good prognosis who can avoid adjuvant chemotherapy.

In our Institute, we obtained a 70-gene signature (MammaPrint) on 116 early breast cancer patients.

Forty-eight patients had a MammaPrint result not useful for clinical decision about adjuvant chemotherapy because 3 were ductal carcinoma *in situ*, 25 (21%) had quality of samples not sufficient to perform the MammaPrint assay and 20 had both oestrogen- and progesterone-receptors negative and then patients were candidates for chemotherapy regardless of the MammaPrint results.

In the remaining 68 cases (58%) both clinical risk and MammaPrint risk were considered for decision making about adjuvant treatment. All cases were discussed in the Breast Disease Management Team with the presence of medical oncologists, surgeons and pathologists.

In 20 (17%) cases clinical risk was discordant with MammaPrint risk. In these cases decision about chemotherapy was based on clinical-pathological factors and disagreed with MammaPrint risk.

In four cases change in clinical decision was based on MammaPrint risk and MammaPrint led to add chemotherapy in all four patients. All these patients had node-negative and hormonal responsive breast cancer with a Ki-67 labelling index greater than 20%.

In addition we observed a slight increase of median Ki-67 value in MammaPrint high risk patients (38%, 12%-94%) versus low risk patients (20%, 4%-82%).

The use of MammaPrint is indicated for patients in which the choice of adjuvant chemotherapy is more difficult as the patients with node-negative and hormonal responsive disease. We used Mammaprint results in only four patients with these characteristics and these results led to add chemotherapy in all patients and to avoid chemotherapy in no patient.

A58 EFFICACY AND SAFETY OF ORAL METRONOMIC CHEMOTHERAPY IN ELDERLY PATIENTS WITH TRIPLE NEGATIVE METASTATIC BREAST CANCER

Russo I., De Iuliis F., Di Trapani M.C., Roselli A., Trasatti L., Pellegrini P., Marchetti P.

Sant'Andrea Hospital, University of Rome "La Sapienza", Italy

Background. Metastatic breast cancer in triple negative patients should be treated until disease progression or unacceptable toxicity. At present there are no standard guidelines about the best treatment in this setting, especially in elderly patients. Objective of this experience is to evaluate the role of metronomic chemotherapy in triple negative patients as first line.

Materials and methods. We have treated from 2009 to 2011 twenty elderly women (age >70 yrs) with metastatic breast cancer. The metastatic sites were: lung (20 patients), liver (10 patients), bone (9 patients), brain (3 patients). Ten patients were treated with capecitabine 1500 mg/m^2 daily, 10 patients with cyclophosphamide 50 mg once daily and methotrexate 2.5 mg twice-weekly.

Results. All patients were evaluable for toxicity and for response. Toxicity was: grade 1 asthenia (100%), grade 1 neutropenia (50%), grade 1 nausea (40%), grade 2 nausea (20%), grade 1 diarrhea (10%). Disease control, defined as stable disease (SD) and overall response (RP), has been: 15 SD and 5 RP after three months of therapy. All the patients received therapy for other three months, evaluating also the progression disease (PD), obtaining these results: 5 PD, 10 SD, 5 RP. Fifteen patients among SD and RP received therapy for other 3 months with these results: 10 SD, 5 PD. After one year we have found 8 SD and 2 PD. The median of duration response was 9 months. The treatment

was safe and well tolerated. None required an interruption in treatment or was hospitalised during the period.

Conclusions. Oral metronomic therapy is a good solution for triple negative metastatic breast cancer in elderly women, with encouraging efficacy and tolerability.

A59 P53 EXPRESSION: PREDICTIVE ROLE IN LOCALLY ADVANCED BREAST CANCER (LABC) TREATED WITH NEOADJUVANT CHEMOTHERAPY. A SINGLE CENTER EXPERIENCE

Giardina G., Oriani A., Vallini I., Milani K., Bini G., Marcon I., Ghizzi M., Pinotti G.

Medical Oncology Unit, Ospedale di Circolo, Varese

Background. p53 is a tumour suppressor protein that is involved in preventing cancer. It plays a role in apoptosis, genomic stability, and inhibition of angiogenesis. In breast cancer, mutation of p53 is often observed and can be involved in cell sensitivity to cytotoxic agents. We studied the possible predictive and prognostic role of p53 in patients (pts) treated with neoadjuvant chemotherapy.

Patients characteristics. From 2004 up to now, we retrospectively analyzed p53 expression at diagnostic core biopsy with immunohistochemistry in 35 consecutively pts with LABC. Pathologic complete response (pCR) was defined as complete disappearance of tumour in breast and nodes. Mean age 43 yrs (range 24-78). 71.5% of pts were ER+ve; 57.5% of pts were PgR+ve. HER-2 was over-expressed in 26% of the cases.

Results. P53 was over-expressed in 28 patients (range 0-99%, mean expression: 48%). All pts had started a neo-adjuvant chemotherapy, 2 patients were ongoing. All pts were treated with TAC regimen. Forty pts underwent surgery. 23% of the patients achieved a pCR, 70% pPR, 7% SD. Median p53 was 54% (range 2%-100%) in pCR patients and 25% in pPR (range 0-98%). At a median follow-up of 44 months, only 3 patients had a relapse. Their p53 was 2% and 95%. One value was not analyzed.

Conclusion. Our study suggests that p53 expression could have a predictive role in response to chemotherapy. The presence of p53 is associated with higher probability of achieving a pCR. Largest clinical studies are needed to confirm these results.

A60 SNPs AND DOCETAXEL RESPONSE IN ADVANCED BREAST CANCER

De Iuliis F., Russo I., Di Trapani M.C., Botticelli A., Gentile G., Simmaco M., Trasatti L., Roselli A., Pellegrini P., Marchetti P.

Sant'Andrea Hospital, University of Rome "La Sapienza", Italy

Background. Taxanes are the most active agents for treatment of breast cancer. Docetaxel is metabolized by CYP3A4 and CYP3A5 and is a substrate for the ATP binding cassette multidrug transporters ABCB1. The impact of genetic aspects on taxane response and survival is unclear: only several studies did not find relationships between polymorphisms of genes in the taxane pathway. The aim of our study was to evaluate the association between genetic assessment and taxane response in patients affected by advanced breast cancer.

Materials and methods. We studied 50 patients affected by advanced breast cancer and under treatment with docetaxel; we genotyped them for selected polymorphisms and ABC-transporters that may influence cellular sensitivity to taxanes: CYP3A4* 1B (A >G), CYP3A5* 3 (G >A) and ABCB1 (1236 C >T; 3435 C >T). SNPs (single nucleotide polymorphism) were characterized by pyrosequencing. Genotypes were investigated for their association with tumour response and survival. The clinical response was determined by RECIST criteria. The statistical survey was conducted by SPSS 14.2 software.

Results. We observed a significant association between patients homozygous for ABCB1 polymorphisms and better clinical outcomes and survival after chemotherapy with docetaxel. We can demonstrate a trend toward longer OS in patients with TT genotype than in those with CC/CT genotype, even though in absence of statistical significance. CYP3A4 and CYP3A5 were not associated with clinical outcomes in terms of objective response and survival.

Conclusion. Our study suggested that genetic polymorphism of ABCB1 C3435T might be associated with improved clinical outcomes in patients treated with docetaxel for stage IV breast cancer. Functional analysis and longer follow-up need to show better the clinical impact of ABCB1 gene polymorphisms.

A61 OUTCOME OF PATIENTS (PTS) WITH HER2+ METASTATIC BREAST CANCER (MBC) TREATED WITH CONTINUOUS INHIBITION OF HER2 ACTIVITY

Fedele P., Orlando L., Schiavone P., Calvani N., Marino A., Nacci A., Sponziello F., Mazzoni E., Rizzo P., Cinefra M., Cinieri S.

Medical Oncology & Breast Unit, "A. Perrino" Hospital, Brindisi, Italy

Background. Anti-HER2 therapies are effective in HER2+ breast cancer; even if resistance occurs, continued HER2 inhibition is required for antitumour effect. There are no definitive data on the clinical benefit of continued trastuzumab (T) beyond progression in MBC and the optimal duration of T in pts with long-term control of disease. This study explores outcomes of MBC pts treated with T in multiple sequential lines.

Methods. From 2001 to 2009 we evaluated OS and cardiac toxicity in 50 pts with HER2+ (ASCO/CAP criteria) MBC who received T-based therapy for ≥12 months. OS was measured from the beginning of T-based CT to the last follow-up visit or death. Cardiac event was any decline in LVEF by >10% from baseline or drop to <50%, III/IV NYHA CHF, new onset angina myocardial infarction, significant arrhytmias or sudden cardiac death.

Results. Median age was 59 (33-79), visceral disease in 60% and multiple site in 34%; 8 (16%) pts developed brain metastases during T. All had overexpression of HER2 by IHC, FISH was centrally assessed in 78% and not amplified in 8%. T was administered for a median duration of 23 months (12-120). All pts received a median of 2 CT regimens (1-8); 9 out of 25 pts with endocrine responsive disease received endocrine therapy plus T after at least 1 CT regimen; 20 pts (40%) experienced CR and received T alone as maintenance for a median duration of 9 months

(3-46); 23 (46%) pts received lapatinib, when the drug was licensed in Italy, after failure of at least two T-based CT lines. Median OS was 34 months (12-120). There were 3 cardiac events (6%) and consisted in asymptomatic decrease in LVEF to less than 50%; T-based CT was interrupted in 1 patient because of LVEF decrease to ≤40%.

Conclusions. T in multiple sequential lines demonstrated highly favorable outcomes in MBC pts. Overall the incidence of cardiac dysfunction was low.

A62 CARDIAC SAFETY OF ANTHRACYCLINE-CONTAINING ADJUVANT CHEMOTHERAPY OF EARLY BREAST CANCER: OSCAR/ABC ONGOING, OBSERVATIONAL, MULTICENTRIC STUDY

Ricevuto E.[1], Cocciolone V.[1], Zilli M.[2], Scognamiglio M.T.[2], Pistilli B.[3], Di Menna G.[2], Mancini M.[4], Cannita K.[1], Adinolfi M.I.[1], Ferrandina M.G.[5], Pancotti A.[6], Recchia F.[7], Latini L.[3], Ficorella C.[1], Iacobelli S.[2] on behalf of CINBO, OSCAR/ABC Investigators

[1]Medical Oncology, San Salvatore Hospital, University of L'Aquila, L'Aquila; [2]Oncologic Clinic, SS. Annunziata Hospital and G. Bernabeo Hospital, University G. D'Annunzio, Chieti-Pescara; [3]Medical Oncology, Ospedale Civile of Macerata, Macerata; [4]Medical Oncology, F. Renzetti Hospital, Lanciano (Chieti); [5]Department of Obstetrics and Gynecology, Catholic University of the Sacred Heart, Rome (Campobasso); [6]Medical Oncology, Mazzini Hospital, Teramo; [7]Medical Oncology, Ospedale Civile of Avezzano, Avezzano (L'Aquila)

Background. Different chemotherapeutic options are available for adjuvant treatment of early breast cancer (EBC). Anthracycline-containing regimens represent prevalent choices. OSCAR/ABC is an observational, prospectic, multicentric study aimed at evaluating, in the clinical practice, the relevance of cardiac dysfunction and congestive heart failure induced by "free choice", selected anthracyclines-containing adjuvant regimens and to identify at-risk patients.

Patients and methods. EBC patients candidate to receive adjuvant anthracycline-containing chemotherapy will be enrolled in the study. Data on demographic and clinical characteristics of the patients (age, comorbidity), tumour features (TNM, histotype, ER and PgR status, Ki67, and HER2 status) and type of adjuvant regimen, will be collected and registered centrally at the Consorzio Interuniversitario Nazionale per la Bio-Oncologia (CINBO) using an e-CRF. Primary objective is to evaluate the prevalence of cardiac dysfunction, particularly according to risk criteria and in HER2 -positive patients. Assessment of cardiac risk involves the evaluation of cardiovascular comorbidities at diagnosis. Cardiac safety and general toxicity on treatment will be evaluated according to NCI criteria. Clinical and instrumental cardiac evaluation (ECG, ecocardiography) will be performed at study entry, on treatment and up to 5 years thereafter. Expected enrollment: 1,200 patients in 24 months. From September 2010 to May 2011, 7 of 13 Centers are active, with 63 patients entering into the study. Preliminary data on cardiac safety will be reported.

A63 EFFECT OF THE MAGNESIUM PIDOLATE IN PATIENTS TREATED WITH AROMATASE INHIBITORS AND ARTHRALGIA SYNDROME. FIRST DATA UPDATE

Prestifilippo A., Mafodda A., Mare M., Blanco G., Munaò S., Vitale M.P., Giuffrida D.

Istituto Oncologico del Mediterraneo, Viagrande, Catania

Background. Aromatase inhibitors therapy (AI) is widely used in adjuvant endocrine treatment in postmenopausal women with early breast cancer. Arthralgia syndrome (AS) is an adverse effect of AI and can be a reason for treatment discontinuation. To date the exact mechanism of arthralgia remains unclear, but may be related to estrogen deprivation. Treatment options for AS are currently inadequate. In clinical practice, higher incidence of hypomagnesaemia was found in patient treatment with AI. The objective of our study is to investigate the potential benefit of implementation of magnesium in the management of this side effect.

Methods. We administered magnesium pidolate (MP) to a group of 50 postmenopausal women with early breast cancer during adjuvant hormone treatment whit AI and AS. The posology of MP was 4.5 g for day for 10 days every 30 and was repeated continuously for 6 months. The evaluation of articular pain due to the treatment was evaluated by a questionnaire. The treatment was already performed again after 6 months in patients with symptom reduction. Calcium concentration and magnesium amount in the blood and urine were evaluated.

Results. We treated a total of 66 postmenopausal patients between 52 and 75 years old. We obtained improvement of the symptoms in 60% of patients impacting their quality of life. There wasn't a significant difference in clinical outcome in relation to serum baseline and urinary calcium and magnesium.

Conclusions. Ongoing studies have evaluated the efficacy of acupuncture, exercise and herbal supplements to improve the AS. This study was limited to a small number of patients and lacks a control group, nevertheless the majority of patients treated with MP showed benefit from the treatment and continued the adjuvant hormonal treatment. Once further data will be available, we suggest to stratify patients in different groups according to the clinical benefit achieved and to indentify co-features in each group of patients, considering also other factors related to AS.

A64 PLASMA D-DIMER LEVELS DO NOT CORRELATE WITH LYMPH NODES INVOLVEMENT IN OPERABLE BREAST CANCER

Fregoni V.[1], Regolo L.[2], Fotia V.[1], Milani A.[1], Pagani A.[1], Da Prada G.A.[1], Zambelli A.[1], Baiardi P.[1], Zanini V.[2], Villani L.[3], Pavesi L.[1], Riccardi A.[1]

[1]Division of Oncology, [2]Division of Breast Surgery, [3]Division of Pathology, IRCCS Salvatore Maugeri Foundation, Pavia, Italy

Background. Malignancy is often accompanied by activated coagulation, underlying a hypercoagulable state. In operable breast cancer, elevated D-dimer end-product plasma levels, reflecting enhanced fibrin formation and fibrinolysis, have been suggested to correlate with tumour stage and axillary nodes involvement. However conflicting results have been recently reported and scanty data are available in the case of single sentinel node biopsy.

Aim. To investigate the possible correlation between D-dimer levels and axillary nodes involvement in operable breast cancer patients.

Patients and methods. Between January 2007 and October 2010, preoperative D-dimer levels were evaluated in 142 consecutive operable breast cancer, receiving axillary lymph node dissection, either preoperatively planned (41 pts) or after sentinel node biopsy (SNB) (101 pts).

Results. The mean D-dimer level of the whole series was 241.71 ng/mL (SD 126.94 ng/mL). Although in the whole series there was a trend for D-dimer levels to be higher in patients with positive lymph nodes with respect to patients with negative lymph nodes, the difference was no statistically significant, considering both the 41 patients who underwent preoperatively planned axillary dissection and the 101 patients who underwent axillary dissection following SNB investigation.

Conclusion. The lack of statistical correlation between D-dimer plasma level and nodes involvement does not support the hypothesis that D-dimer might be related to breast cancer clinical stage.

A65 LAPATINIB IN COMBINATION WITH CAPECITABINE IN HER2 POSITIVE METASTATIC OR ADVANCED BREAST CANCER AFTER FIRST-LINE TRASTUZUMAB

Ghiani M., Valle E., Farci D., Gutmann G., Urracci Y., Piga A.

Medical Oncology, Ospedale Oncologico A. Businco, Cagliari

Aim. Lapatinib is a small molecule dual tyrosine kinase inhibitor, selective for inhibition of epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor 2 (HER2), licensed for the use in association with capecitabine in HER2 positive metastatic or advanced breast cancer after first-line trastuzumab-based chemotherapy. It gained regulatory approval in April 2009. We describe here our experience since the approval until April 2011.

Methods. From July 2009 to April 2011, 28 patients were treated at our Institution with the approved schedule lapatinib and capecitabine. Patients, in pre- or postmenopausal status, had visceral, bones or both metastatic sites; all patients had previously received trastuzumab in association with chemotherapy or hormonal therapy. One patient, for whom regulatory agency authorization was obtained, had been treated with capecitabine. Response evaluation was performed after 3 months of treatment with CT scan or PET-CT. Cardiological assessment was performed before start of treatment and after 4 months.

Results. Twenty-one out of 28 patients received at least 3 months of treatment; of these, 7 had PR, 13 SD and 1 PD; 5 patients were not evaluable for response (early death or therapy refusal), 2 patients have not yet reached 3 months of therapy. Median TTP was 6.5 months. Decrease in serum markers predicted duration of response. Ten patients are still on treatment, two at 14 months from start and one at 11 months. Although diarrhea and rash were common, no grade 3 toxicity was recorded.

Conclusion. The combination of lapatinib and capecitabine was in our experience manageable, with no relevant side effects, with good disease control and long lasting responses in HER2 positive metastatic or advanced breast cancer after first-line trastuzumab based chemotherapy. In the vast majority of patients therapy with trastuzumab could be resumed at progression.

A66 IMPACT ON QUALITY OF LIFE OF ORAL THERAPIES ON METASTATIC BREAST CANCER PATIENTS. COMBINATION OF ORAL CAPECITABINE AND VINORELBINE

Arcanà C.*, Ingemi M.C.*, Guerrera M.°, Berenato F.*, Smiroldo V.*, Spadaro P.*

**Oncology Unit, °Psycho-Oncology Unit, Casa di Cura Villa Salus, Messina, Italy*

The purpose of this study was to assess impact on quality of life (QoL) and tolerability profile of metastatic breast cancer (MBC) patients (pts) treated in our institution with an all-oral combination schedule of capecitabine (Cape) and vinorelbine (VNR).

Each 3-week cycle of treatment consisted of 500 mg/m^2 Cape twice daily (2 weeks on, 1 week off), and 60 mg/m^2 VNR on days 1 and 8.

Sixty pts were included. Median age was 49 years (range 33-73). Forty-two pts (70%) had a performance status (PS) ECOG 0; 12 pts (20%) PS 1 and 6 pts (10%) a PS 2. Fifty pts (83%) previously received adjuvant (adj) hormonal therapies and/or adj/neoadj chemotherapy. Twelve pts (20%) received Cape + VNR as first metastatic line treatment. Fifty-six pts (93.3%) had more than one metastatic site involved (range 2-4). Median number of cycles was 6 (range 3-16).

We administered a QoL evaluation anonymous questionnaire. Thirty-three pts (55%) completed the interview. Twenty pts (60%) were able to spend their usual day life activities. Twenty-eight pts (84%) declared to feel "less sick" with non-infusional therapies. Fifteen pts (45%) pointed out the importance of not worrying families when less access in hospital needed. Thirty pts (90%) underlined psychological impact of "keeping all hairs in head"; 30 pts (90%) were satisfied of the treatment chosen. Three pts (10%) reported "a sense of medical neglect" and difficulty to "keep in contact with the trustworthy physician"; 1 pt (3%) stopped treatment for "having the impression of doing nothing just taking pills".

Toxicity profile: 36 pts (59.7%) referred nausea G1; 14 pts (23.2%) vomiting G1; 28 pts (46.5%) asthenia G1-G2; 22 pts (36.5%) G1-G3 diarrhea; 1 (1.6%) alopecia G1. Thirteen pts (21.5%) experienced G1-G3 "hand and foot syndrome". Hematological toxicity: 24 (39.8%), neutropenia G1-G2: 1 (1.6%) requiring treatment discontinuation; 11 (18.6%) anemia G1 and 14 (23.2%) thrombocytopenia G1-G2.

Oral combination of Cape and VNR favourably impacts on QoL of MBC pts and has a good tolerability profile.

A67 VINORELBINE AND CAPECITABINE REGIMEN IN METASTATIC BREAST CANCER (MBC) PATIENTS: A PHASE II STUDY

Porrino P., Bergnolo P., Chiadò Cutin S., Dal Canton O., Boglione A., Oliva C., Pochettino P., Garetto F., Monasterolo G., Ottaviani D., Inguì M., Comandone A.

S.C. di Oncologia, Presidio Sanitario Gradenigo, Torino

Backround. Vinorelbine and capecitabine are worldwide recognized as active agents in MBC. The aim of this phase II study was to evaluate the activity and the feasibility of capecitabine and oral vinorelbine as second- and third-line chemotherapy in patients with metastatic breast cancer (MBC) previously treated with anthracycline and/or taxanes containing regimens.

Patients and methods. From 2008 to 2011, 20 patients received a schedule consisting of oral vinorelbine 60 mg/m^2 on days 1 and 8 plus capecitabine 1000 mg/m^2/bidie from days 1 to 14, both given every 3 weeks. The mean age was 59, median 60 (range 41-60). All patients had previously received antracyclines, 80% of patients taxanes; 15 pts (75%) had received prior CT for MBC. Median PS ECOG 1 (0-2). The median number of administered cycles per patients was 5 (range 1-10). Sites of metastases were: hepatic 3 pts (15%), lung 6 pts (30%), lymph nodes 8 pts (40%), cutaneous 3 (15%).

Results. All pts were assessable for toxicity and 18 (90%) for response. The schedule was well tolerated, only one patient developed grade 3 toxicity: constipation. Five pts (25%) had grade 2 leukopenia, 4 (20%) hand-foot syndrome; nausea and vomiting were recorded in 7 pts (35%), fatigue grade1-2 in 6 pts (30%). Four (20%) pts obtained a partial response, 3 pts (15%) disease stabilisation and 11 (55%) disease progression. The reasons for non evaluability were in one case the premature discontinuation for toxicity after one cycle and in the other because the therapy is ongoing. Median time to progression was 4.5 months.

Conclusions. Oral vinorelbine and capecitabine represent a well tolerated regimen and offer an all oral treatment. For these reasons, the schedule is a good option for second-line therapy and for elderly patients.

A68 THE PATIENT WITH BREAST IMPLANTS FOLLOWING CANCER: IMPACT ON THE BODY IMAGE AND ON THE QUALITY OF LIFE

Zito S.[1], Cirio L.[1], Pirro E.[2], Storto S.[3], Ciuffreda L.[3], Lorenzi E.[4], Balestra L.[4], Dimonte V.[5], Mussa M.V.[1]

[1]School of Nursing, University of Turin, Italy; [2]Laboratory of Clinical Pharmacology, Department of Clinical & Biological Sciences, University of Turin, AOU San Luigi Gonzaga, Orbassano, Italy; [3]Oncology Ward, AOU San Giovanni Battista, Turin, Italy; [4]Breast Unit, AOU San Giovanni Battista, Turin, Italy; [5]Department of Hygiene and Public Health, University of Turin, Italy

Objectives. The aim of the study was to assess the body image perceived by women and the impact on their quality of life, after breast reconstruction with implants in two stages.

It also attempted to assess whether or not there are correlations between some characteristics of women and their degree of aesthetic satisfaction.

Methods. The study considered a sample of 49 women with a mean age of 54 years, SD ± 11.004, 30 with temporary tissue expander and 19 with permanent prosthesis.

To achieve the objectives was administered a questionnaire referring to EORTC QLQ-C30 (version 3.0), SF-36 and the Body Image Scale.

Results. Differences were statistically significant, analyzing the following groups of variables: the presence in the breast of temporary tissue expander or permanent prosthesis ($p = 0.04978$), to have or not children ($p = 0.04941$), a different period of time spent by the intervention of mastectomy ($p = 0.00015$), the type of mastectomy ($p < 0.00001$) and the reconstruction or less of the nipple-areola complex ($p = 0.03029$).

Conclusions. Analysis of the results shows how the two-stage breast reconstruction with implants is viewed positively by patients. They identify it as a way to restore the altered body image, appreciate once again their femininity and get back to carry out daily living activities as before the intervention of mastectomy.

With the progress of the reconstruction process, thus by increasing time spent after mastectomy, by having breast permanent prosthesis rather than expander and having reconstructed nipple-areola complex, the breast takes on a more natural appearance, affecting positively women about their body image.

A69 TREATMENT EFFECT OF BISPHOSPHONATES IN THE PREVENTION OF SKELETAL EVENTS IN BREAST CANCER PATIENTS WITH OSTEOPOROSIS

Tanca F.M.[1], Madeddu C.[1], Astara G.[1], Massa E.[1], Ruggiero V.[2], Floris C.[3], Spiga C.[3], Mudu C.[4], Valle E.[5], Pisano A.[5], Gramignano G.[6], Mela Q.[7], Montaldo L.[7], Cotti E.[8], Dettori C.[8], Mantovani G.[1]

[1]Department of Medical Oncology, [2]Department of Rheumatology, University of Cagliari, Cagliari; [3]Operative Unit of Medicine, Nuova Casa di Cura, Decimomannu (Cagliari); [4]Medical Oncology Service, Polispecialistica Sant'Elena, Casa di Cura Kinetika Sardegna s.r.l, Quartu Sant'Elena (Cagliari); [5]Department of Medical Oncology, Ospedale Oncologico Regionale A. Businco, Cagliari; [6]Department of Medical Oncology, Ospedale Nostra Signora di Bonaria, San Gavino Monreale (VS); [7]Department of Internal Medicine, [8]Department of Conservative Dentistry, University of Cagliari, Cagliari

Objectives. To assess efficacy and safety of zoledronic acid in breast cancer patients receiving adjuvant hormone therapy with osteoporosis and at high risk of skeletal events.

Methods. Open prospective non-randomized phase II study. Eligibility criteria: histologically confirmed estrogen-receptor positive breast cancer; range 18-75 years; stage I-III; any grading; osteoporosis; adjuvant hormone therapy with tamoxifen ± LHRH analogues or aromatase inhibitors. At baseline all patients underwent the following assessments: DEXA, orthopantomography and dental examination; blood levels of VEGF, IL-8, IL-6, TNF-alpha, lymphocytes sub-populations, bone alkaline phosphatase, osteocalcin, osteopontin, osteonectin, N- and C-terminal telopeptides, bone sialoprotein, vitamin D, PTH, calcemia, phosphoremia (screening). Eligible patients were then treated with zoledronic acid (5 mg once/year) for two years. The above evaluations were repeated monthly in year 1and every 3 months in year 2. Preliminary results. Forty-six patients, all female, underwent the preliminary interview and 31 completed the screening: 12 were eligible (3 of them did not give their consent to participate to the study). Out of the 12 eligible patients, all postmenopausal, 2 had stage I, 8 stage IIA, 1 stage IIB, 1 stage IIIA; 3 had negative and 9 positive lymph nodes; 10 underwent quadrantectomy + homolateral lymphadenectomy and 2 radical mastectomy; 3 had c-erb-B2 positive tumours and received trastuzumab; all patients underwent adjuvant radiotherapy and are receiving letrozol; 9 received anthracycline-based adjuvant chemotherapy (3 of them in association with taxanes); 4 had already received oral bisphosphonates.

Conclusions. The present abstract reports preliminary data relating to screening phase. The study is ongoing.

A70 NON PEGYLATED LIPOSOMAL DOXORUBICIN (NPLD) IN NEOADJUVANT TREATMENT OF LOCAL ADVANCED BREAST CANCER (LABC)

Vari S.[1], Tomao F.[2], Rossi L.[1], Spinelli G.P.[1], Ricci F.[3], Lo Russo G.[1], Papa A.[1], Stati V.[1], Giordani E.[1], Strudel M.[1], Zoratto F.[1], Tomao S.[1]

[1]Department of Medical-Surgical Science and Biothecnology, Oncology Unit, S. Maria Goretti Hospital, Latina, University of Rome "Sapienza"; [2] Department of Obstetrics and Gynecology, University of Rome "Sapienza"; [3]Department of Surgery, S. Maria Goretti Hospital, Latina

Background. Anthracyclines are active in treatment of breast cancer, but their use is limited by cardiac toxicities. Development of nPLD has resulted in an improved safety profile and comparable efficacy to conventional anthracyclines. Aim of this experience in a small number of patients is to evaluate the safety and efficacy, in neoadjuvant setting, of nPLD in patients with LABC.

Patients and methods. All patients were confirmed for histological diagnosis of c-erbB2 negative invasive ductal carcinoma G3, one patient was triple negative, no previous cardiovascular diseases and no other neoplasia and LVEF >55%. Median age was 46 years (range 40-52). Seven patients were enrolled, CT Total Body, mammography, echography and breast MRI were used to clinical staging: cT2 cN0 (n = 1), cT3 cN0 (n = 1), cT4 cN0 (n = 1), cT4 cN2 (n = 3) and cT4 cN3 (n = 1); all patients were cM0. Docetaxel was administered at a dose of 75 mg/m^2, cyclophosphamide 500 mg/m^2 and nPLD 50 mg/m^2 every 3 weeks for 4 cycles. All patients received primary prophylaxis with G-CSF. After 4 cycles all patients were restaged and made a surgical reassessment. Patients in clinical response but not yet eligible for surgery received other chemotherapy cycles and then a new revaluation. A total of 31 cycles and a median of 4.4 cycles were administered.

Results. Only one patient interrupted treatment after one cycle for liver and cardiological toxicities. Radiological responses were: 1 complete response, 4 partial response and 1 stable disease. No disease progression was observed. Six patients were submitted to surgery. Histological exams showed: ypT1a ypN0 (n = 2); ypT1b ypN0 (n = 1); ypT4 ypN1 (n = 1); ypT4 ypN0 (n =1); and ypT4 ypN3 (n = 1). Primary toxicity observed was nausea G3 (n = 4); only two cases of neutropenia G4. No LVEF decreased >10% and no congestive heart failure were observed.

Conclusions. Despite the small number of patients, our experience suggests a manageable safety profile and efficacy of nPLD in neoadjuvant settings for LABC.

A71 PACLITAXEL WITH BEVACIZUMAB (PB) AS FIRST-LINE THERAPY FOR METASTATIC BREAST CANCER: OUR EXPERIENCE

Salesi N., Di Cocco B., Colonna M., Veltri E.S.A.

U.O.C. Oncologia Sud ASL Latina, Ospedale "Di Liegro", Gaeta (LT)

Background. In a clinical trial of 722 patients (pts) with locally recurrent metastatic breast cancer (MBC) solvent-based paclitaxel 90 mg/m^2 (wPac) was administered intravenously (IV) over 1 hr weekly for 3 weeks followed by a week of rest (q3/4w) alone or in combination with bevacizumab (Bev) 10 mg/kg every 2 weeks (q2w) (E2100 Trial). As compared with single agent, the combination had a greater median progression-free survival (PFS; 11.4 months (mo) vs. 611 mo, p <0.0001) and overall response rate (ORR; 30% vs 14%, p <0.0001).

Methods. We reviewed data for 16 patients: pts ≥20 years with HER2-negative measurable MBC, ECOG PS ≤1 and no prior chemotherapy for MBC, received Bev 10 mg/kg d1 and d15 with wPac 90 mg/m^2, d1, 8, and 15 q4w, as in E2100 trial. Co-primary endpoints were time to progression (TTP) and safety. Secondary endpoints included ORR (RECIST v1) and overall survival (OS).

Results. A total of 16 patients were registered and evaluated between June 2009 and September 2010. Median age: 68 (32-76); postmenopausal: 80%; baseline ECOG <2 100% of patients. Metastatic sites were lung (45%), nodes (60%), liver (47%), pleura (35%), bone (47%). Two patients (12.5%) achieved CR, 6 (37.5%) PR (ORR 50.0%) and 8 (50.0%) SD; the median FU was 9 (range 2.5-16.0) mo, the median time to progression 9.6 mo. The median survival was 20.3 mo and the probability of 1-year survival 71.3%. Main grade 3-4 toxicities: neutropenia (31.5%). A total of 115 cycles were administered (median: 6 cycles/patient).

Conclusion. The Bev-wPac combination in our experience showed high activity, similar to that seen in E2100 trial. No new safety signals were seen in this population.

A72 BREAST ADENOMYOEPITHELIOMA: A CASE REPORT WITH MALIGNANT PROLIFERATION OF EPITHELIAL AND MYOEPITHELIAL ELEMENTS

Pasciuti G.[1], Sardella B.[2], Tomao F.[1,5], Pacchiarotti A.[3], Miraglia A.[2], Rossi L.[1], Censi F.[2], Veccia N.[2], Di Cristofano C.[2], Petrozza V.[2], Fontana A.[4], Della Rocca C.[2]

[1]Department of Medical-Surgical Science and Biotechnology, Oncology Unit, S. Maria Goretti Hospital, Latina, University of Rome "Sapienza"; [2]Department of Experimental Medicine, Pathology Unit, ICOT, Latina, University of Rome "Sapienza"; [3]San Marco Clinic, Pathology Unit, Latina; [4]Department of Radiotherapy, S. Maria Goretti Hospital, Latina; [5]Department of Obstetrics and Gynecology, University of Rome "Sapienza"

Background. Breast adenomyoepithelioma is an unusual benign tumour characterized by biphasic proliferation of epithelial and myoepithelial cells. Most breast adenomyoepitheliomas are considered to be benign or to have a low grade malignant potential, characterized by propensity for local recurrence. Malignant changes arising in this lesion are extremely rare and may involve one or both cellular components.

Case report. We discuss a case of a 60 years old female. In January 2009 appearance of pain in the right breast. Breast ultrasound and mammography were performed showing in right QII a rounded, hypoechoic solid lesion with ill-defined margins, in part suspicious of malignancy. Chest radiograph and liver ultrasound did not show any evidence of metastatic disease. Quadrantectomy QII of right breast with sampling of ipsilateral axillary lymph nodes was performed. Lymph nodes did include any metastatic lesions. On microscopic section showed a fairly circumscribed gray-white, lobulated tumour with two distinct morphological areas. Histological examination established the diagnosis of adenomyoepithelioma with focal malignant change of epithelial component associated with local malignant change of myoepithelial component. Immunohistochemical studies were carried out with epithelial and myoepithelial markers. The significant areas of the tumour were positive for CK7, p63, S100, CK5, CK 6 and CK14. Grade of the tumour was high. Patient was treated with adjuvant

radiotherapy and right breast received a dose of 50 Gy with a boost of 10 Gy on the tumour bed.

Conclusion. Breast malignant adenomyoepithelioma is a rare tumour which should be considered in the differential diagnosis of a solid breast lesion. Only few cases have been reported in literature and establishing the diagnosis, determining the optimal therapy and predicting outcome are problematic because of the rarity of this disease. It appears to have hematogenous rather than lymphatic spread and usually occurs in primary tumours more than 1.5 cm in size.

A73 PROOF OF THE ANTI-TUMOUR EFFECT OF ZOLEDRONIC ACID (ZA) IN NAÏVE BONE-ONLY METASTATIC AND LOCALLY ADVANCED BREAST CANCER (LABC): RESULTS FROM THE "BIOLOGICAL WINDOW THERAPY"

Foroni C.*, Andreis D.*, Maldotti M.*, Cortellazzi C.*, Boni E.*, Santini D.§, Berruti A.^, Damia G.°, Bottini A.*, Generali D.*

**U.O. Multidisciplinare di Patologia Mammaria, Laboratorio di Oncologia Molecolare Senologica, A.O. Istituti Ospitalieri di Cremona; ^Dipartimento di Scienze Cliniche e Biologiche, Università degli Studi di Torino, Oncologia Medica Azienda Ospedaliera San Luigi; °DNA Repair Unit, Istituto di Ricerche Farmacologiche "Mario Negri"; §Divisione di Oncologia Medica, Campus Biomedico di Roma*

Background. Pre-clinical studies have demonstrated an anti-tumour activity of ZA in several cancers. However, the clinical evidence of the ZA anti-tumour effect is still uncertain. Our study aimed to prove that ZA has anti-tumour activity administered alone as a biological window of 14 days therapy on naïve bone-only metastatic and LABC.

Material and methods. Twenty-seven patients with LABC (Group 1) and 12 patients at their first relapse with bone metastasis only (Group 2) received 4 mg single dose of ZA before starting any treatment. In Group 1, Ki67 expression was evaluated in tumour specimens obtained before and after ZA administration (basal, day 14). In Group 2, circulating tumour cells (CTCs) were evaluated at baseline, 48 hrs and day 14. In Group 1 and 2, the apoptosis and necrosis of tumour cells were tested on blood samples by M30 and M65 ELISAKit respectively. Parallely, the anti-antitumour activity of ZA, given at the dose of 250 mg/mouse every 4 days for 6 cycles, in MDA-MB-231 bearing mice was evaluated.

Results. A significant reduction of Ki67 expression after 14 days (mean 25.33% to 21.78%; $p = 0.035$) was observed in Group 1. In Group 2, we detected a significant reduction of CTC number after 48 hrs (median 16 to 7; $p = 0.045$), followed by a tendency to increase on day 14 ($p = 0.093$). The M30/M65 analysis performed on paired blood samples in Group 2 showed after 14 days a significant increase in M65 (median 97 to 112 U/L; $p = 0.018$), more accentuated than the concomitant increase in M30 ($p = 0.308$). In MDA-MB-231 bearing mice, ZA treatment caused a significant inhibition of tumour growth.

Conclusions. These results are the first prospective clinical data showing a direct anti-tumour effect (either on the tumour or on CTCs) of ZA, confirming the *in vitro* data. By directly affecting the proliferation, ZA could have an anti-tumour effect via induction of necrosis, suggesting its possible use in combination with conventional oncologic treatments of breast cancer.

A74 A RARE CASE OF PITUITARY METASTASES FROM BREAST CANCER

Lo Russo G.[1,2], Spinelli G.P.[1,2], Tomao F.[3], Papa A.[1], Giordani E.[1], Prinzi N.[4], Miele E.[4], Stati V.[1,2], Basso E.[1], Tomao S.[1,2]

[1]Department of Medical-Surgical Science and Biotechnology, Oncology Unit, S. Maria Goretti Hospital, Latina, University of Rome "Sapienza"; [2]Distretto ASL Aprilia, Oncology Unit, University of Rome "Sapienza"; [3]Department of Obstetrics and Gynecology, University of Rome "Sapienza"; [4]Department of Experimental Medicine, University of Rome "Sapienza"

Introduction. Pituitary metastases are an uncommon complication of cancer. Their rarity and the lack of specific radiological and clinical signs limit their differentiation from other more common benign pituitary lesions. We present a case of late recurrence of breast cancer occurred with bone metastasis and with a pituitary metastatic mass.

Case report. In November 1998 a 73 years old woman underwent quadrantectomy with axillary lymph node dissection for infiltrating ductal carcinoma of right breast (NOS variant, G1, pT1c, pN0, ER +, PgR +). Thus the patient was treated with tamoxifen for 5 years. The follow-up controls were negative for recurrence until June 2010, when diagnosis of bone metastasis was evidenced and the patient started treatment with letrozole. In October 2010 visual disturbances appeared and magnetic resonance imaging (MRI) of the pituitary region revealed a sellar mass compressing the optic chiasm. This lesion was about 11 mm of diameter and was compatible with pituitary adenoma. It was confirmed by endocrinological findings that showed the presence of panhypopituitarism. In January 2011 due to a progressive deterioration of visual disturbances (bitemporal hemianopsia), a new brain MRI with gadolinium was executed. It evidenced an enlargement of mass volume and an infiltration of optic chiasm. Despite the probably metastatic nature of the lesion, surgical decompression and biopsy were performed. Histology showed a malignant neoplasm compatible with metastatic breast cancer. Because of rapid clinical deterioration of the performance status no other treatments were performed.

Conclusion. The purpose of the alert to this rare clinical case is primarily to emphasize the importance of careful follow-up, especially in breast cancer. It should also be underlined the real need for a correct differential diagnosis between benign and malignant lesions of the pituitary region.

A75 NEOADJUVANT CHEMOTHERAPY IN STAGE IIIB BREAST CANCER: HOW IS THE BETTER SCHEDULE? A MONOINSTITUTIONAL PHASE II STUDY

Cotroneo G., Rodà G., Galdy S., Mauri C., Galmozzi A., Iaculli A., Bonassi L., Duluc M., Nastasi G.

U.O. Oncologia Medica, A.O. Bolognini, Seriate (BG)

Background. Neoadjuvant chemotherapy for locally advanced breast cancer is given with the aim of shrinking the disease sufficiently for surgery. However, many clinical trials investigating neoadjuvant chemotherapy regimens were conducted for operable breast cancer.

From the review of several case studies in the literature, re-

sponse rate is equal to 60-90%, with a clinical complete response rate ranging from 6 to 65%. Actually the optimal chemotherapy regimen is not known but it seems that the taxanes provide a better response rate.

Aim. Response rates were determined according to RECIST criteria. Toxicity was graded according the National Cancer Institute's common toxicity criteria.

Patients and methods. Twelve patients (pts) were enrolled between Jan/2008 and Jan/2010. Baseline characteristics include: median age 51 (range 45-66); ECOG PS 0, stage IIIB ductal breast carcinoma. Ten pts (6 ER+, HER2-; 1 ER-, HER2+; 3 ER+, HER2+) received PEV schedule: epirubicin 75 mg/m^2 iv, cisplatin 50 mg/m^2 iv, vinorelbine 25 mg/m^2 g1 q21 continuously 3 cycles; 2 pts (1 ER-, HER2+; 1 ER+, HER2-) received TEC schedule: docetaxel 75 mg/m^2 iv; epirubicin 75 mg/m^2 iv and cyclophosphamide 500 mg/m^2 iv continuously 3 cycles with primary prophylaxis with pegfilgrastim at day 2. All patients were offered support from our psychologists.

Results. Six patients had demonstrated partial response (RR 50%, 4 with PEV regimen and 2 with TEC regimen). Stable disease was documented in 4 pts (RR 33.4%), 2 pts had a minimal response (16.6%). The most common toxicities were haematological toxicities (one grade IV and one grade III, not febrile neutropenia in TEC subsetting without delay or dose reduction); nausea and vomiting were observed in 4 pts in PEV subsetting (no grade III-IV toxicities); only one neurotoxicity (grade III) was demonstrated in TEC subsetting. There were no negative effects of this treatment regimen on quality of life assessments.

Conclusions. In our esperience TEC schedule had more hematological toxicities, while PEV schedule had more gastroenteric toxicities like vomiting. Four patients were treated with quadrantectomy but for residual disease underwent mastectomy. Two patients despite the good response rate underwent mastectomy for extensive residual disease (initial tumour size 7 and 11 cm respectively).

A76 LONG-TERM PATIENT WITH BREAST CANCER SURVIVORS: EVALUATION OF QUALITY OF LIFE

Casciaro R.[1], Cirio L.[1], Pirro E.[2], Storto S.[3], Ciuffreda L.[3], Lorenzi E.[4], Grietti E.[4], Passarella G.[4],Verbale M.[4], Dimonte V.[5], Mussa M.V.[1]

[1]School of Nursing, University of Turin, Italy; [2]Laboratory of Clinical Pharmacology, Department of Clinical & Biological Sciences, University of Turin, AOU San Luigi Gonzaga, Orbassano, Italy; [3]Oncology Ward, AOU San Giovanni Battista, Turin, Italy; [4]Breast Unit, AOU San Giovanni Battista, Turin, Italy; [5]Department of Hygiene and Public Health, University of Turin, Italy

Objective. The aim of this study was to identify any issues of quality of life of long-term survivors cancer patients (surviving for not less than 4-5 years from diagnosis) in order to propose long-term solutions through multidisciplinary programs.

Materials and methods. The study considered a sample of 42 women, defined long-term survivors with a diagnosis of breast cancer, who underwent surgery and subsequently were treated with radiotherapy, chemotherapy and adjuvant hormonal therapy. The questionnaires that evaluate life quality (EORTC QLQ-C30 and QLQ-BR23) were given to patients treated at the Breast Unit of AOU San Giovanni Battista (Turin).

Results. Analysis of the results is statistically significant. Evidence was found in the area of sexuality related to body image and emotions.

Conclusions. The results obtained are compliant to literature. In fact these patients refer problems related to sexuality in relation to their body perception and to the consequent psychological impact for long-term disease and treatment received.

A77 RADIOLOGICAL AND PATHOLOGICAL COMPLETE RESPONSE IN A YOUNG PATIENT LOCALLY ADVANCED HER2 BREAST CANCER AFTER NEOADJUVANT TREATMENT WITH TRASTUZUMAB AND NON-PEGYLATED LIPOSOMAL DOXORUBICIN (nPLD)

Papa A.[1], Rossi L.[1], Vari S.[1], Zoratto F.[1], Lo Russo G.[1], Pasciuti G.[1], Ricci F.[2], Giordani E.[1], Rinaldi G.[1], Spinelli G.P.[1], Tomao F.[1,3]

[1]Department of Medical-Surgical Science and Biothecnology, Oncology Unit, S. Maria Goretti Hospital, Latina, University of Rome "Sapienza"; [2]Department of Surgery, S. Maria Goretti Hospital, Latina; [3]Department of Obstetrics and Gynecology, University of Rome "Sapienza"

Background. nPLD has been shown to offer a significant decrease in cardiotoxicity when compared with doxorubicin while preserving doxorubicin-associated antitumour efficacy. In patients with HER2-overexpressing breast cancer, trastuzumab has been shown to be effective when associated with chemotherapy. However, cardiotoxicity is one of the main adverse events which have been observed with trastuzumab use. Trastuzumab and nPLD could be a powerful combination with a non-significant risk of cardiotoxicity.

Case report. Patient of 40 years without comorbidities. In September 2010 appearance of a lump in ISQ of left breast with skin ulceration. In ISQ mammography, breast ultrasound and MRI describe an hypervascular area of 6.4 x 2.4 cm with confluence of multiple nodules (Dmax = 2 cm). In the ipsilateral axilla were hyperplastic lymph nodes (Dmax = 1.5 cm). Staging tests negative for distant metastasis. Pre-treatment LVEF = 70%. Tumour markers were negative. Incisional biopsy was positive for ductal carcinoma infiltrating superficial dermis, hormone receptor positive, c-erbB2++ by IHC. Initial staging cT4b cN0 cM0. In November 2010 began chemotherapy with docetaxel (75 mg/m^2)-nPLD (50 mg/m^2)-cyclophosphamide (500 mg/m^2), p1q21 days and with G-CSF support. After two cycles docetaxel has been suspended due to severe allergic reaction. At FISH determination c-erbB2 resulted amplified; then we replaced nPLD with trastuzumab (8 mg/kg first, 6 mg/kg later) for a total of four cycles. Re-staging tests were negative for distant metastasis. Mammography, breast ultrasound and MRI give evidence of radiological complete response. Post-treatment LVEF = 68%. Quadrantectomy of ISQ and sentinel lymph node biopsy were performed with histology: ypTx ypN0sn.

Conclusion. In this patient, combination of trastuzumab and nPLD proved to be a very effective therapeutic strategy. In fact we obtained a radiological and pathological complete response despite only 4 cycles of trastuzumab. Association has also been shown to be safe and well tolerated in absence of short-term cardiotoxicity.

Association of trastuzumab and nPLD in neoadjuvant setting could be a safe therapeutic option, mainly for patients not suitable for treatment with other more cardiotoxic anthracyclines.

Session B • Gynaecological tumours

B1* PREDICTIVE VALUE OF 18F-FDG-PET/CT IN LOCALLY ADVANCED CERVICAL CARCINOMA TREATED WITH NEOADJUVANT CHEMOTHERAPY

Ippolito M.[1], Cosentino S.[1], Baldari S.[1], Murè G.[1], Scopelliti F.[1], Sabini M.G.[1], Scibilia G.[2], Banna G.L.[2], Fraggetta F.[3], Parisi A.[2], D'Agate G.[2], Lipari H.[2], Scollo P.[2]

[1]Department of Nuclear Medicine, [2]Divisions of Gynecology and Oncology, Maternal-Infant Department, [3]Service of Human Patology, Cannizzaro Hospital, Catania, Italy

Background. To evaluate the predictive value of SUV (standardized uptake value) for locally advanced cervical cancer treated with neoadjuvant chemotherapy.

Methods. Patients aged 18 to 75 years, with FIGO stage IB2-IIB cervical cancer, treated with 3 cycles of neoadjuvant paclitaxel, ifosfamide and cisplatin (TIP) chemotherapy, followed by radical surgery, were evaluated by 18F-FDG-PET/TC scan 1 week before the start of chemotherapy and 21 days after the third cycle. SUV max and delta SUV were measured. For tumour response assessment, a comparison with abdomen MRI and post-surgical histopathology was performed.

Results. Twenty-five patients (median age 53 years, range 28-75) were assessed from January 2008 to March 2009. Fifteen out of 25 patients (60%) showed a correlation with clinical FIGO stage; 9 (36%) were ruled out for the detection of node and distant metastasis; 1 (4%) did not show 18F-FDG uptake. A complete response was observed in 5 patients (33%) (average SUV max pre-TIP 9.8; delta SUV -100); a partial response in 8 (53%), 5 (33%) with minimal residual disease (>3 mm, <7 mm) (average SUV max pre-TIP 13; delta SUV -95.8) and 3 (20%) with more than minimal residual disease (average SUV max pre-TIP 9.9; delta SUV -38); a stable disease in 2 (13%) (average SUV max pre-TIP 8.2; delta SUV -5.7).

Conclusions. Delta SUV by 18F-FDG-PET, but not SUV max value at the baseline, showed good correlation with histological response to neoadjuvant chemotherapy, thus supporting the role of 18F-FDG-PET in the assessment of tumour response for locally advanced cervical cancer. The 18F-FDG-PET may also have an important role for initial disease staging.

B2* THE COMBINATION OF WEEKLY CARBOPLATIN AND PACLITAXEL IS ACTIVE AND TOLERATED FOR THE TREATMENT OF ADVANCED OVARIAN CANCER IN ELDERLY PATIENTS

Lugini A.[1], Rossi R.[2], Pace R.[1], Rauco A.M.[1], Sciacca V.[2], Pistillucci G. [2], Capparella V.[1]

[1]Medical Oncology, Ospedale Generale "San Camillo de Lellis", Rieti, Italy; [2]Medical Oncology, Ospedale "Santa Maria Goretti", Latina, Italy

Background and aims. Platinum/taxane doublets have long been considered the standard treatment regimen for advanced stage ovarian cancer. Common side effects seen with the use of these drugs include gastrointestinal symptoms, myelosuppression and neurological toxicity. The purpose of this study was to evaluate feasibility, effectiveness, toxicity and quality of life of a weekly schedule, containing carboplatin and taxanes in elderly patients.

Methods. From January 2009 to December 2010, 24 patients (pts) with advanced ovarian cancer were included in the study. Median age was 74 years, and PS was 1, 2 and 3 in 15, 6 and 3 patients respectively. The pts received carboplatin AUC 2 (day 1, 8, 15), and paclitaxel 80 mg/m^2 (days 1, 8, 15) of a 28-day cycle. Primary endpoints were response rate, progression-free survival and overall survival. The results were retrospectively analyzed according to feasibility, toxicity (National Cancer Institute Common Toxicity Criteria) and quality of life (QoL).

Results. All patients were evaluable for the primary endpoint. The overall response rate was 80% (14 complete responses, 5 partial responses); the median survival has not yet been reached after a median follow-up of 24 months. Toxicity was: neutropenia grade 2/3 (33.3%); nausea grade 2 (40%); grade 1 vomiting (5%). No patient reported a worsening of QoL referable to the side effects of treatment.

Conclusions. A weekly carboplatin and paclitaxel regimen is highly active for women with advanced stage ovarian cancer. The regimen is well tolerated in elderly patients.

B3* EMA-CO CHEMOTHERAPY FOR HIGH-RISK GESTATIONAL TROPHOBLASTIC TUMOURS

Tavella K.[1], Villanucci A.[1], Busi E.[2], Mertino P.[2], Vannini L.[2], Gatto S.[2], Amunni G.[3]

[1]Unit of Medical Gynaecologic Oncology, Department of Oncology, AOU-Careggi, Florence, Italy; [2]Department of Health of Woman and of Child, AOU-Careggi, Florence, Italy; [3]University of Studies of Florence, Italy

Objectives. To evaluate the applicability of EMA-CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) therapy for the treatment of high-risk gestational trophoblastic tumours (GTT) and low-risk GTT non responders to methotrexate treatment.

Methods. Between 1980 and February 2011, 22 patients with FIGO-defined high-risk or low-risk GTT non responders to methotrexate received EMA-CO treatment.

Results. EMA-CO therapy was administered to 13 patients with high-risk GTT as first-line treatment, to 9 patients with low-risk as second-line treatment. One patient with choriocarcinoma in low-risk, underwent EMA-CO treatment as primary therapy only.

A total of 116 cycles of EMA-CO was administered to these patients.

Twenty patients achieved a complete remission, 2 patients died. These two patients experienced recurrence of disease.

The only grade 4 toxicity experienced by patients was the hematologic toxicity. 9.1% of the patients developed grade 4 leukopenia, 13.6% of the patients developed grade 4 neutropenia, 4.5% of the patients developed grade 4 anemia. 22.7% of the patients developed grade 3 leukopenia. 63% of patients developed grade 3 alopecia.

Conclusions. According to our clinical observation multiagent therapy with EMA-CO is the gold standard treatment for high-

risk GTT and for low-risk non responders to single agent therapy. Its toxicity is manageable. None of the chemotherapy schedules was changed because of the toxicity.

B4* GENE EXPRESSION KNOCKDOWN OF *CASC2A* INDUCES A GROWTH ADVANTAGE IN HUMAN ENDOMETRIAL CANCER

Baldinu P.[1], Dessole S.[2], Mara L.[3], Tanda F.[4], Palmieri G.[1]

[1]Unità di Genetica dei Tumori, Istituto di Chimica Biomolecolare, CNR, Sassari; [2]Dipartimento Ostetricia e Ginecologia, Università di Sassari; [3]Istituto Zootecnico e Caseario per la Sardegna, Olmedo (SS); [4]Istituto di Anatomia Patologica, Azienda Ospedaliero-Universitaria, Sassari, Italy

Background. Our group previously demonstrated that *CASC2a* is involved in pathogenesis of endometrial cancer (EC). Exogenous expression into completely undifferentiated endometrial cancer cells indicated that *CASC2a* may be classified as a tumour suppressor gene. In this study, we decided to perform the opposite experiment on Ishikawa well differentiated human endometrial adenocarcinoma cells by silencing *CASC2a*.

Methods. Long-term *CASC2a* gene expression knockdown in Ishikawa cells was assessed by stable transfection with pSilencer 4.1-CMV puro siRNA expression vector containing short hairpin interfering RNAs (shRNAs). Ishikawa cells were transfected with pSilencer-CASC2a shRNAs (designated as ISH-TS4) or pSilencer negative control vector (designated as ISH-PURO) containing a non-functional shRNA but conferring the puromycin resistance.

Results. Firstly, ISH-TS4 and ISH-PURO cell lines were screened for *CASC2a* expression levels by real-time RT-PCR. Pooling data from all stable transfectants obtained in triplicate experiments, ISH-TS4 showed a significant decrease (more than 50%) in *CASC2a* expression as compared to the *CASC2a* endogenous levels in ISH-PURO cells. Considering the total number of colonies >100 μm (per 10,000 cells seeded), ISH-TS4 cell lines formed colonies with a frequency much higher than that calculated for ISH-PURO (colony formation ratio between ISH-TS4 and ISH-PURO, 18:1).

Conclusions. *CASC2a* down-regulation was demonstrated to provide a growing advantage to well differentiated EC cells, conferring the ability to form colonies under anchorage-independent conditions. *CASC2a* has thus confirmed to act as a tumour suppressor gene.

B5* POSITRON EMISSION TOMOGRAPHY (PET) IN PATIENTS (PTS) WITH METASTATIC OR LOCALLY ADVANCED CERVICAL CANCER (CC)

Murgia V.[1], Caffo O.[1], Bagatin E.[2], Caldara A.[1], Magri E.[3], Vanoni V.[3], Galligioni E.[1]

[1]U.O. Oncologia medica, [2]U.O. Medicina Nucleare, [3]U.O. Radioterapia, Ospedale S. Chiara, Trento

Background. The prognosis of CC is related to primary tumour stage, size, histologic grade, and to the lymph nodes status. It has been hypothesized that some PET parameters such as tumour uptake of fluorine-18-labeled fluorodeoxyglucose (18FDG) measured as maximum standardized uptake value (SUVmax) and tumour volume may be associated with aggressive biological characteristics of cancer cells, in patients with CC. The present report is aimed to evaluate the prognostic role of PET in CC patients treated with chemotherapy (CT) alone and concurrent chemo/radiotherapy (CT/RT).

Methods. Between January 2007 and November 2010, a consecutive series of 24 pts with CC was treated with CT or CT/RT. All pts underwent a baseline 18FDG PET/TC. For each assessment we evaluated SUVmax, while metabolic tumour volume (cervix and lymph node) was measured by an automated contouring program with a fixed threshold of SUV max = 2.5.

For each patient we also recorded traditional prognostic factors (histology, tumour grade, smoking status, age, and stage). Progression-free survival (PFS) and overall survival (OS) were calculated by Kaplan-Meier methods.

Results. Major pts characteristics were: median age 54 yrs (range 33-77); median PS 0 (range 0-2); smokers 17 and no smokers 7; FIGO stage: Ib2 in 2 pts, IIa in 1, IIb 4, IIIb in 7, IVa in 4, IVb in 6. Histology: squamous in 21 pts and adenocarcinoma in 3.

No statistically significant relationship was found between PET parameters and traditional prognostic factors, excepting for stage with earlier stages (I-III) having a lower tumour volume compared to patients with IV stage (58.77 vs 136.5 mm^3, p = 0.031). Similarly, PFS and OS were not influenced by PET parameters.

Conclusions. From our preliminary data, PET parameters are not able to distinguish pts with different prognosis. Anyway, PET may increase our ability of tumour measuring. Larger samples are necessary to definitively assess the prognostic value of PET in CC.

B6 NEOADJUVANT POLICHEMOTHERAPY (PCT) WITH IFOSFAMIDE, PACLITAXEL AND CISPLATIN REGIMEN IN LOCALLY ADVANCED SQUAMOCELLULAR CARCINOMA OF THE CERVIX. A PHASE II STUDY IN OUR INSTITUTION

Rodà G., Galmozzi A., Mauri C., Cotroneo G., Iaculli A., Duluc M., Bonassi L., Nastasi G.

U.O. Oncologia Medica, A.O. Bolognini, Seriate (BG)

Background. Surgery, radiotherapy or sometimes both were the best treatments for locally advanced cervical cancer beyond womb such as vagina, sides of the pelvis or nearby lymph nodes. The exact choice of treatment would have depended on the size and location of the tumour and the preferences of the woman and her doctor. Nowadays, women with this type of cancer may be given combined chemotherapy and radiotherapy at the same time. Or, they may have surgery as well as this combined chemotherapy and radiotherapy. However, giving neoadjuvant chemotherapy might have a similar benefit, but have less side effects than giving the treatments at the same time.

Aim. To determine the response rate of locally squamocellular carcinoma of the cervix; to describe toxicities associated with this regimen.

Patients and methods. From March 2009 to December 2010 we enrolled 10 eligible patients (pts) with histologically locally

advanced squamocellular carcinoma of the cervix not amenable to curative treatment with surgery and/or radiation therapy. PCT was given 21-day cycle: mesna (3000 mg/m^2) plus ifosfamide (3000 mg/m^2) in continuously 24 hours iv infusion from day 1 to day 3, paclitaxel (175 mg/m^2) day 1, cisplatin (50 mg/m^2) day 1 and primary prophylaxis with lenograstim from day 4 to day 8. Response rates were determined according to RECIST criteria. Toxicity was graded according the National Cancer Institute's common toxicity criteria. All patients were offered support from our psychologists.

Results. Ten patients participated in this study, with 9 evaluable for response rate. One patient died after severe metabolic decompensation in diabetic; 6 pts (66.7%) had a demonstrated objective response (2 complete responses, 4 partial responses). Stable disease was documented in 3 pts (33.3%). Bone marrow suppression was the most common toxicity (no grade III/IV haematological toxicities); nausea and vomiting were observed in 4 pts (no grade III-IV toxicities); only one neurotoxicity (grade III) was demonstrated in the diabetic patients. There were no negative effects of this treatment regimen on quality of life assessments.

Conclusions. Ifosfamide, paclitaxel and cisplatin is an effective regimen in treating locally advanced squamocellular carcinoma of the cervix and has an acceptable toxicity profile.

B7 PHASE II STUDY OF LOW DOSE BEVACIZUMAB IN HEAVILY PRETREATED PATIENTS WITH EPITHELIAL OVARIAN CANCER

Defferrari C., Campora S., D'Amico M., Piccardo A., Biscaldi E., Repetti F., Pasa A., Puntoni M., Gozza A., Gennari A., Zanardi S., De Censi A.

S.C. Oncologia Medica, Medicina Nucleare, Radiologia, Ginecologia, E.O. Ospedali Galliera, Genova

Background. Bevacizumab is a potent angiogenesis inhibitor that has been shown to prolong PFS in the first-line treatment of epithelial ovarian cancer (EOC).

The purpose of this study was to assess the safety and activity of low-dose bevacizumab in combination with carboplatin or oral cyclofosfamide in heavily pretreated advanced stage ovarian carcinoma.

Patients and methods. We treated 15 patients with epithelial ovarian cancer, stage III-IV, 13 (87%) had serous and 2 (13%) endometrioid histology, median age 60 years, median ECOG PS = 0. The patients received a median number of four prior cytotoxic regimens (range 3-5). Ten (66%) were considered platinum resistant and five (33%) partially sensitive. Treatment consisted of bevacizumab 5 mg/kg q21 (10 patients) or 7.5 mg/kg q21 (5 patients) in combination with carboplatin AUC2 weekly or AUC6 q21 or oral cyclofosfamide 50-100 mg/day. Bevacizumab was administered until disease progression.

The median number of bevacizumab cycles was 21 (range 3-59).

Results. Grade 3 adverse events related to bevacizumab were hypertension (2) and proteinuria (1).

Epistaxis was noted in 5 cases. The treatment was never stopped for toxicity, was delayed in five patients for bleeding (2) and uncontrolled hypertension (3). No grade 4 toxicity was observed.

The median baseline CA125 was 272.0 ng/mL and 15.20 at nadir. Median PFS was 21 months.

Tumour response by CE-CT with PET and colography is being evaluated by RECIST and PERCIST criteria.

Conclusions. In this heavily pretreated population bevacizumab seems to be well tolerated and active based on PFS and CA125 levels. The high tolerability, the low incidence of proteinuria and hypertension suggest that this regimen can be administered in heavily pretreated advanced-stage ovarian cancer.

B8 PRES IN PATIENT WITH VESICULAR MOLE: A CASE REPORT

Villanucci A.[1], Tavella K.[1], Mertino P.[2], Vannini L.[2], Busi E.[2], Ladu C.[3], Mannelli E.[3], Amunni G.[4]

[1]Unit of Medical Gynaecologic Oncology, Department of Oncology, [2]Department of Health of Woman and of Child, AOU Careggi, Florence, Italy; [3]School of Specialization in Anaesthesia and Reanimation, University of Studies of Florence, Italy; [4]University of Studies of Florence, Italy

Gestational trophoblastic tumours (GTT) are very rare (1/1000 pregnancies and only the 20% of those tumours will be treated by chemotherapy) diseases that are closely linked to a pregnancy.

Our case report describes the clinical story of a young woman, sixteen years old, that received a curettage of uterus because of a vesicular mole of second degree (characterized by a high production of beta-HCG: 1.105.317 U/mL); then her clinical picture was complicated by the appearance of neurologic symptoms like sight troubles, cephalea, recurring epileptic crisis. Because of those symptoms and thanks to other checks it was possible to diagnose a posterior reversible encephalopathy syndrome (PRES) that has been treated by using a multidisciplinary therapy. She had also lung metastases. After the acute phase, our patient received five chemotherapy cycles of EMACO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) regimen chosen according to the WHO classification. After the negativization of beta-HCG obtained with those five chemotherapy cycles, our patient received other two cycles for consolidation obtaining a complete remission of disease included lung metastases. She well tolerated the chemotherapy treatment, without important complications.

B9 DEVELOPMENT OF ENDOMETRIAL CANCER AND THE DISAPPEARANCE OF THE UTERINE CERVIX AFTER RADIATION TREATMENT FOR CERVICAL CANCER: EFFECT OF RADIATION TREATMENT? A CASE REPORT

Lapadula L.[1], Capobianco A.M.L.[2], Martinelli G.[3], Vita G.[4], Cammarota A.[5], Aieta M.[2], Fusco V.[1]

[1]Radiotherapy Unit, [2]Oncology Unit, [3]Gynecology Unit, [4]Anatomopathology Unit, [5]Radiology Unit, IRCCS-CROB, Rionero in Vulture (PZ), Italy

Background. In literature there are reports of patients treated with radiotherapy alone for invasive carcinoma of the cervix who then have developed endometrial cancer.

Purpose. The purpose is to signal not only the development of a second tumour but also the absence of actinic alterations in the uterine body that have allowed a histological diagnosis of en-

dometrial cancer and especially the absence of the uterine cervix after exclusive radiation treatment ten years before.

Methods and results. Woman aged 75 treated in 2001 with radiotherapy alone (BOX conformal with X 6 MV, DT 50, 4 Gy DF 180 cGy + Intracavitary BRT HDR ^{192}Ir DT 18 Gy, DF 600 cGy I FR weekly + Parametrial Boost AP-PA with security-central DT 10 Gy DF 200 cGy) for poorly differentiated carcinoma of the cervix stage IIB (TNM-V ed.).

The patient came to our attention in March 2011 for ematometra after 10 years of negative follow-up. The MRI abdomen-pelvis showed that the uterine cavity contained a large content partially corpusculated and no evidence of cervix.

The patient underwent radical hysterectomy with bilateral annexectomy and pelvic lymphoadenectomy. The macroscopic examination showed an uterus with no cervix. In numerous samples on the uterus histological examination shows a chronic inflammation and in this context the presence of poorly differentiated carcinoma with papillary growth pattern, tubule compatible with solid and cystic compatible with endometrial origin, immunophenotype CK7+, CK20-, WT1-, Vimentina+, p53+(90%), ER-, PgR-, CEA+, infiltrating the inner layer of the myometrium, stage pT1a pN0 (TNM-VII ed.), FIGO IA. Actinic changes are not evident at the level of the uterine body.

Conclusions. The endometrial tumours that arise after the exclusive RT on the cervix are rare, late and with more aggressive histologies. This case report wants to focus on the growth of a second tumour of the endometrium, but especially on the disappearance and not atrophy of the cervix due to radiation therapy (RT), that should preserve the specific organ.

B10 MALIGNANT STRUMA OVARII: A CASE REPORT

Ricci M.[1], Milandri C.[1], Casadei Gardini A.[1], Riva N.[1], Burgio M.A.[1], Nannini R.[2], Musconi M.[3], Amadori D.[1]

[1]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), Meldola (FC); [2]Unità Operativa Complessa Anatomia Patologica, C/O Polo Sanitario Territoriale di Imola, Ex Ospedale Vecchio (BO); [3]Ginecologia e Ostetricia, Ospedale Santa Maria della Scaletta di Imola (BO)

We present a case of malignant struma ovarii in a 61 years old woman. The patient underwent total thyroidectomy in 1996 with a histological diagnosis of benign colloidocystic multinodular goiter. In February 2011 the patient was submitted to bilateral annexectomy in laparoscopic surgery (4 cm right ovarian cyst). Histological diagnosis was mature cystic teratoma with carcinoid struma. The thyroid component was mixed with a solid cell proliferation of monomorphic appearance positive for synaptophysin and focally positive for chromogranin. Negative staining for calcitonin, Ki67 <1%. The patient underwent thyroid scan, chest, abdomen and pelvic CT scan, hemato-biochemical profile, without significant findings.

In such cases, the patient should be treated as for carcinoma of the thyroid; endocrinological evaluation, thyroidectomy and radioiodine therapy after staging with CT scan to rule out other sites of abdominal disease. Struma ovarii is a rare mature teratoma with predominant thyroid tissue (>50%), showing all the pathologic patterns of the thyroid gland, including malignancy. It is associated with hyperthyroidism in 5-8% of cases and treatment modalities depend on the stage of disease. Standard treatment is total abdominal hysterectomy, bilateral salpingo-oophorectomy, and complete surgical staging, including peritoneal washings for cytology, pelvic and para-aortic lymph node sampling, and omentectomy. In patients with residual malignant disease after surgery, total thyroidectomy and radioablation with 131I are recommended. Adjuvant treatment includes thyroxine, subtotal thyroidectomy with radioactive iodine ablation, or no adjuvant treatment. Although metastases are uncommon (5-23% of cases), long term follow-up is recommended. In our patient, close follow-up was decided because of the previous surgery.

B11 IS THERE A ROLE FOR TARGETED THERAPIES IN THE TREATMENT OF CERVICAL CANCER?

Guadalupi V., Zanaboni F., Grijuela B., De Carrillo A.K., Gabbanini M., Ramondino S., Betto E., Raspagliesi F.

Dipartimento di Ginecologia Oncologica, IRCCS, Istituto Nazionale Tumori, Milano

Cervical cancer represents an important cause of cancer-related death in female population. Standard of treatment of localized disease is surgery.

In locally advanced disease surgery should be performed after neoadjuvant chemotherapy. In high risk patients, the surgical treatment should be followed by chemotherapy, radiotherapy or both.

At surgical failure the antitumoral treatment has a palliative role and it is rarely possible to obtain long-term remission. The drugs considered active have response rates ranging between 20-60%.

Targeted therapy is a generic term to indicate a group of drugs with different mechanism of action. Our objective is to verify by analysis of literature data if it is possible to attribute a role to monoclonal antibodies and tyrosine-kinase inhibitors in the treatment of cervical cancer.

Bevacizumab is one of the first molecular target therapies. It is a recombinant humanized anti-vascular endothelial growth factor (VEGF) monoclonal antibody. Recent studies have investigated the expression patterns of TB-4 (thymosin beta4, related with tumour metastasis and angiogenesis), VEGF and HIF1-alfa.

The expression of these proteins in primary tumours with lymph node metastasis and their metastatic tumours in lymph node were less than in tumours without lymph node metastasis. Those data suggest the potential benefit of bevacizumab in early stage of cervical cancer.

Moreover, many researchers have shown that oncoproteins of human papillomavirus could enhance the vascular endothelial growth factor expression. Therefore, the expression of VEGF could be involved in cervical carcinogenesis.

Cetuximab (Erbitux) is a monoclonal antibody, that inhibits the epidermal growth factor receptor (EGFR). At present several clinical studies with cetuximab in cervical cancer are ongoing, including a study evaluating the efficacy of cetuximab monotherapy in persistent or recurrent carcinoma of the cervix. In previous studies the frequency of EGFR overexpression in cervical cancer has been reported to occur in 6-85%. In conclusion, targeted therapies should play a role in the treatment of cervical cancer in early or advanced disease; however, further studies are necessary to clarify preclinical data.

Session C • Gastrointestinal tumours (colorectal excluded)

C1* THE ROLE OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) AND VEGF RECEPTORS GENOTYPING IN GUIDING THE METASTATIC PROCESS IN RADICALLY RESECTED GASTRIC CANCER PATIENTS

Scartozzi M.[1], Loretelli C.[2], Galizia E.[3], Mandolesi A.[4], Pistelli M.[5], Bittoni A.[5], Giampieri R.[1], Bianchi F.[2], Belvederesi L.[2], Del Prete M.[5], Maccaroni E.[5], Faloppi L.[5], Bianconi M.[5], Berardi R.[1], Bearzi I.[4], Cascinu S.[1]

[1]Clinica di Oncologia Medica, [2]Centro Regionale di Genetica Oncologica, [3]Anatomia Patologica, A.O. Ospedali Riuniti, Università Politecnica delle Marche, Ancona, Italy; [4]Oncologia Medica, Ospedale Profili, Fabriano, Italy; [5]Scuola di Specializzazione in Oncologia, Università Politecnica delle Marche, Italy

In radically resected gastric cancer the possibility to predict the site of relapse could be clinically relevant for the selection of post-surgical management. We previously demonstrated that tumour integrins genotyping is involved in determining the metastatic sites. Tumour angiogenesis may also be crucial for the metastatic process of gastric cancer cells. We then investigated the role of VEGFs and VEGF receptors genotyping in determining either peritoneal carcinosis or hematogenous metastases in radically resected gastric cancer.

Genotyping for VEGF-A, VEGF-C and VEGFR-1, 2, 3 was carried out on pT4a radically resected gastric tumours recurring with either peritoneal only or hematogenous metastases. Tumour genotyping for integrins was also performed

101 patients were analysed: 57 with peritoneal carcinomatosis only and 44 with hematogenous spread only. At multivariate analysis, intestinal histology and the AC genotype of rs699947 (VEGFA) showed to correlate with hematogenous metastases, whereas diffuse histology and the AA genotype of rs2269772 (ITGA) correlated with peritoneal only diffusion (p = 0.001) (Table 1).

Our results suggest that information from genotyping of rs699947 (VEGFA, AC), rs2269772 (ITGA, AA) and tumour histology could allow clinicians to individuate gastric cancer at high risk for recurrence with peritoneal or hematogenous metastases. The selection tool deriving from this analysis may allow an optimal use of the available treatment strategies in these patients.

Table 1

	rs10434 (VEGFA, G >A)			
	GG	GA	AA	ND
Peritoneal carcinosis no. (%)	16 (28)	30 (53)	5 (9)	6 (10)
Hematogenous metastases no. (%)	11 (25)	20 (46)	12 (27)	1 (2)
p	n.s.	n.s.	0.0282	
	rs699947 (VEGFA, A >C)			
	AA	AC	CC	ND
Peritoneal carcinosis no. (%)	9 (16)	17 (30)	26 (45)	5 (9)
Hematogenous metastases no. (%)	5 (11)	26 (59)	11 (25)	2 (5)
p	n.s.	0.006	n.s.	
	rs7993418 (FLT1, A >G)			
	AA	AG	GG	ND
Peritoneal carcinosis no. (%)	34 (60)	16 (28)	1 (2)	6 (10)
Hematogenous metastases no. (%)	21 (48)	13 (29)	7 (16)	3 (7)
p	n.s.	n.s.	0.0259	

C2* A TRIPLE APPROACH STRATEGY FOR PATIENTS WITH LOCALLY ADVANCED PANCREATIC ADENOCARCINOMA

Cantore M.[1], Girelli R.[2], Mambrini A.[1], Frigerio I.[2], Boz G.[3], Lusenti A.[1], Giardino A.[2], Bassi C.[2]

[1]Department of Oncology, Carrara; [2]Hepatopancreatobiliary Unit, University of Verona; [3]Department of Radiotherapy, CRO, Aviano

Background. Patients with locally advanced pancreatic cancer (LAPC) have an expected median survival ranging from 10 to 13 months. New strategies are needed. Radiofrequency ablation (RFA) is an emerging and feasible procedure to treat patients with LAPC, radiochemotherapy (RCT) seems to increase local control and intra-arterial/systemic chemotherapy (IASC) can reduce liver progression.

Methods. At our Institutions, patients with LAPC were treated with RFA; RCT (twice-weekly gemcitabine 40 mg/m^2 administered concurrently with external beam radiation therapy at a dose of 54.0-59.4 Gy) and IASC (epirubicin 35 mg/m^2 and cisplatin 42 mg/m^2 on day 1 every 4 weeks, combined with systemic gemcitabine 1000 mg/m^2 on day 2, and capecitabine 650 mg/m^2/bid over 14 days) were combined with RFA, in a triple approach strategy (TAS).

Results. Between February 2007 and June 2010, 107 patients with LAPC were treated with RFA. RCT was performed in 88 patients; IASC in 35; combination of RFA plus RCT plus IASC (TAS) in 32. After a median follow-up of 25.7 months, median overall survival (OS) was 25.6 months, with 1-year and 2-year survival of 76% and 52%, respectively. Patients submitted to TAS had an OS of 34.0 months (1- and 2-year survival of 97% and 80%). In univariate analysis, performance status (0 vs 1, OS 39.9 vs 18.4 months), RCT (yes vs no, OS 31.5 vs 14.2 months), IASC (yes vs no, OS 35.1 vs 16.5 months) and TAS (yes vs no, OS 34.0 vs 18.4 months) were significant predictors of survival. Among patients treated with TAS, 3 were submitted to laparotomy (10%) and showed a patological complete response. Multivariate analysis revealed three independent significant variables: performance status, RCT and IASC.

Conclusions. Observed survival of 25.6 months from diagnosis appears unexpected in a group of 107 consecutive patients with LAPC. Multimodality approach identify a subgroup of 32 patients submitted to TAS with an impressive survival of 34 months. It urgely needs further evaluations to confirm these results.

C3* INTENSIVE UP-FRONT TREATMENT VS A SEQUENTIAL APPROACH IN ADVANCED GASTRIC CANCER PATIENTS: DOES FIRST-LINE MATTER?

Pistelli M.[1], Scartozzi M.[2], Bittoni A.[1], Galizia E.[3], Giampieri R.[1], Maccaroni E.[1], Faloppi L.[1], Bianconi M.[1], Del Prete M.[2], Berardi R.[2], Cascinu S.[2]

[1]Scuola di Specializzazione in Oncologia, Università Politecnica delle Marche, Italy; [2]Clinica di Oncologia Medica, AO Ospedali Riuniti, Università Politecnica delle Marche, Ancona, Italy; [3]Oncologia Medica, Ospedale Profili, Fabriano, Italy

Aims and background. The definition of the standard chemotherapy regimen for advanced gastric cancer is still a matter of debate. A recent meta-analysis suggested that the addition of a third drug to a doublet regimen should be considered the state-of-the-art strategy to improve overall survival. Aim of our analysis was to retrospectively assess whether an intensive, three-drugs, front line approach could be comparable to a sequential (two-drugs front line then second-line) in terms of RR (response rate), PFS (progression-free survival) and OS (overall survival) in advanced gastric cancer patients.

Methods. Patients with locally advanced or metastatic gastric cancer who have received a first-line combination chemotherapy with a two or three-drugs regimen were included in our analysis. We divided our patients into two groups, A and B, based on the first-line chemotherapy administered (group A = three drugs; group B = two drugs).

Results. A total of 390 patients were eligible for our analysis. 211 patients (54%) received three chemotherapeutic agents (group A) and 179 patients (46%) received a two drugs regimen as first-line combination chemotherapy (group B). The 2 groups of patients resulted comparable for all known prognostic factors of clinical relevance. RR for group A and B was 46.7% and 28%, respectively ($p = 0.0007$), median PFS was 7.12 months in group A and 3.96 months in group B ($p < 0.0001$). No significant difference resulted for the median OS of patients in the two groups (13 months for group A and 11.8 months for group B; $p = 0.962$).

Conclusions. The addition of a third drug to a doublet chemotherapy regimen appeared more active in terms of response rate and PFS. However median OS resulted comparable. On this basis, a triplet regimen may represent an optimal chance, particularly when response and PFS are relevant treatment endpoints. Nevertheless the use of a sequential approach may also represent a reasonable strategy for patients unwilling or unable to undergo a more intensive treatment without compromising OS.

C4* SECOND LINE RAD001 IN BILIARY TRACT CANCER (BTC) PATIENTS (PTS): A PHASE II ITMO STUDY

Buzzoni R.[1], Pusceddu S.[1], Biondani P.[1], Aitini E.[2], Cantore M.[3], Alabiso O.[4], Bertolini A.[5], Niger M.[1], Ciarlo A.[6], Bajetta E.[7] on behalf of ITMO (Italian Trials in Medical Oncology) group

[1]Medical Oncology Unit 2, Fondazione IRCCS "Istituto Nazionale dei Tumori", Milan, Italy; [2]Medical Oncology, Azienda Ospedaliera "C. Poma"di Mantova; [3]Medical Oncology, ASL 1 Massa e Carrara; [4]Medical Oncology, Ospedale Maggiore della Carità, Novara; [5]Medical Oncology, Ospedale di Sondrio; [6]Medical Oncology, ASL 4, Presidio Ospedaliero Prato; [7]Oncology Institute, Policlinico di Monza

Background. The incidence of BTCs is increasing, reporting a slightly better prognosis in cholangiocarcinoma vs gallbladder. Results are disappointing both after radical surgery and with front line standard chemotherapies. Survival in the metastatic setting is in the range of only a few months. The search for new therapeutic options is a challenge to ameliorate prognosis and quality of life. RAD001 (Everolimus), an emerging m-TOR inhibitor has been studied as antineoplastic agent in solid tumours in phase I-II trials. Findings suggest that BTC pts might benefit from RAD001 treatment.

Methods. From February 2009 to December 2009, 39 pts were enrolled in a multicentric phase II study with the aim to assess the efficacy (disease control rate, tumour progression) and safety of oral RAD001 10 mg daily/28 day cycle. A biomarker study was planned to correlate mTOR expression and antitumour activity. All the pts, progressing after front line chemotherapy were enrolled according to a Simon two stage design. Eligibility criteria also included performance status ECOG ≤2, adequate organ function and absence of clinically significant cardiovascular disease.

Results. Patient median age 63 yrs, male/female = 22/17, ECOG 0/1/2 = 31/5/3. No toxic death was reported. Thrombocythemia was the main haematologic side effect in 35% (G3 4 pts), followed by neutropenia in 15% (G3-G4 2 pts). Stomatitis appeared in 20% (G3 1 pt). A CR and a PR lasting 9 and 10 months respectively were reported. Disease control rate was achieved in 45% of cases. On the entire group TTP was about 3 months but in 25% TTP exceeded 5 months. Long lasting SD (>6 months) was reported in 19.4% of cases.

Conclusions. RAD001 can be safely administered and the evidence of a significant disease control rate in such chemotreated pts is encouraging. More data are needed to support the hypothesis of RAD001 as front line treatment. The correlation between mTOR expression and clinical benefit is an important issue which needs a clarification.

C5* *MET* COPY NUMBER GAIN IMPACTS ON PROGNOSIS OF HIGH RISK GASTRIC CANCER PATIENTS

Graziano F.[1], Galluccio N.[2], Lorenzini P.[3], Catalano V.[1], Andreoni F.[2], Ligorio C.[4], Canestrari E.[2], Sisti V.[5], Ruzzo A.[2], D'Emidio S.[1], Di Oto E.[4], Rulli E.[6], Fiorentini G.[1], Zingaretti C.[5], De Nictolis M.[3], Cappuzzo F.[7], Magnani M.[2]

[1]Division of Medical Oncology, Azienda Ospedaliera "Ospedali Riuniti Marche Nord", Pesaro, Italy; [2]Department of Biomolecular Sciences, University of Urbino, Italy; [3]Department of Histopathology, Azienda Ospedaliera "Ospedali Riuniti Marche Nord", Pesaro, Italy; [4]Section of Histopathology, Ospedale Malpighi, Bologna, Italy; [5]Department of Surgery, Azienda Ospedaliera "Ospedali Riuniti Marche Nord", Pesaro, Italy; [6]Laboratorio Clinical Trials, Istituto di Ricerche Farmacologiche "Mario Negri", Milan, Italy; [7]Department of Medical Oncology, Ospedale Civile di Livorno, Livorno, Italy

Background. A number of receptor and downstream pathways are abnormally activated in gastric cancer (GC) and they may represent new treatment targets beyond HER-2 inhibition. The MET receptor and its hepatocyte growth factor (HGF) ligand were found frequently expressed in gastric carcinomas with more aggressive phenotype. We investigated whether prognosis of high risk GC patients (pts) may depend on *MET* copy number gain (CNG) or an activating truncation in a deoxyadenosine tract element (DATE) in *HGF* promoter.

Methods. A single-institution cohort of 230 radically resected (R0), stage II-III GC pts was studied. Formalin-fixed paraffin-

embedded tumor specimens were used for DNA extraction. Quantitative PCR (qPCR) for *MET* CNG analysis and sequencing for *HGF* DATE truncation (<25 deoxyadenosines instead of 30) were used. Results were analyzed for association with disease-free survival (DFS) and overall survival (OS). To assess the reliability of the qPCR measurements, they were compared with FISH results in 32 random samples, and calculating the intra-correlation coefficient (ICC). The maximum ICC value is 1 and the minimum is 0. The closer the ICC is to 1, the more is the agreement.

Results. In 216 assessable pts, there were 97 relapses (45%) and 94 deaths (43.5%). *MET* CNG was <2 copies in 9 pts (4%), ≥2 to <3 copies in 116 pts (54%), ≥3 to <4 copies in 35 pts (16%), ≥4 to <5 copies in 35 pts (16%) and ≥5 copies in 21 pts (10%). Homozygous *HGF* truncated DATE was found in 30 pts (13%). Pts with *MET* CNG ≥5 copies (*MET*-positive) showed significantly worse prognosis with multivariate HR = 3.2 (95% CI = 1.71-5.33; p .0001) for DFS and multivariate HR = 2.91 (95% CI = 1.65-511; p .0002) for OS. There was high agreement between qPCR and FISH with ICC = 0.9 (95% CI = 0.81-0.95).

Conclusions. This is the first and largest analysis of *MET* CNG in Caucasian GC pts. Pts with *MET* CNG ≥5 copies were about 10% and they showed unfavorable prognosis. This information is relevant to the current clinical development of anti-*MET* compounds.

C6* EVEROLIMUS AND OCTREOTIDE LAR AS FIRST-LINE TREATMENT OF LUNG AND ABDOMINAL NEUROENDOCRINE TUMOURS: AN ITMO (ITALIAN TRIALS IN MEDICAL ONCOLOGY) GROUP STUDY

Bajetta E.[1], Catena L.[1], Biondani P.[2], Fazio N.[3], Giuffrida D.[4], Ricci S.[5], Aieta M.[6], Pucci F.[7], Bianco N.[1], Valente M.[1]

[1]Istituto di Oncologia, Policlinico di Monza, Monza, Italy; [2]Fondazione IRCCS Istituto dei Tumori, Milan, Italy; [3]Istituto Oncologico Europeo, Milan, Italy; [4]Istituto Oncologico del Mediterraneo, Catania, Italy; [5]Azienda Ospedaliera S. Chiara, Pisa, Italy; [6]Ospedale Oncologico Regionale, Rionero in Vulture, Italy; [7]Azienda Ospedaliero-Universitaria, Parma, Italy

Background. Everolimus is an oral inhibitor of mTOR (mammalian target of rapamycin). It has shown antitumour activity in advanced pancreatic neuroendocrine tumours (NETs) and it seems to work synergistically with somatostatine analogues. The primary objective of this multicentric study is to assess the activity and safety of everolimus combined with Octreotide LAR as first-line treatment of advanced neuroendocrine tumours of the lung and the gastro-entero-pancreatic tract.

Material and methods. From March 2009 to June 2010, 50 patients (21 female and 29 male) affected with advanced neuroendocrine carcinoma were treated with everolimus 10 mg/day and Octreotide LAR 30 mg/month, until disease progression and/or unacceptable toxicity. Forty-two pts had a well differentiated endocrine carcinoma of the gastro-intestinal tract and 8 had a typical or atypical lung carcinoid. The median age was 60.5 yrs (range 25-76).

Results. An interim analysis has been performed, and the results about the response rate and toxicity of this combination are as follows:

– the clinical benefit is 96%: SD 83.7%, PR 9.3% and CR 2.3%;

– the mild and moderate adverse events (G1 and G2) were: diarrhoea 12 pts (24%), stomatitis 7 pts (15%), skin rash 13 pts (28%), hypercolesterolaemia 7 pts (14%), hyperglycemia 5 pts (10%), thrombocytopenia 3 pts (6%) and interstitial lung disease in 1 patient (2%). We also reported G3 mucosal inflammation (stomatitis and anal inflammation) in 4 pts (9%), hypokaliemia G3 in 1 pt due to diarrhoea, and stomatitis G4 in only 1 patient. No adverse events leaded to withdrawal from study treatment.

Conclusions. The preliminary analysis shows that the combination seems to be effective not only in pancreatic NETs, as reported, but also in lung and other gastro-entero-pancreatic neuroendocrine neoplasms.

C7 AN OBSERVATIONAL STUDY OF A FOUR-DRUG COMBINATION IN PATIENTS WITH ADVANCED PANCREATIC ADENOCARCINOMA

Reni M., Cereda S., Belli C., Ghidini M., Rognone A., Passoni P., Longoni S., Ceraulo D., Fugazza C., Villa E.

San Raffaele Scientific Institute, Milan

Background. The combination of cisplatin (P), epirubicin (E), 5-fluorouracil (F) and gemcitabine (G) (PEFG regimen) yielded a progression-free at 6 months from treatment start (PFS6) of about 50% and a 1-year overall survival (OS) around 40% in patients with advanced pancreatic adenocarcinoma (PA). Subsequent trials confirmed these figures and suggested that capecitabine (X) may replace F (PEXG regimen). We report the outcome of a single institution series of patients treated with a PEXG regimen in the clinical practice.

Methods. Chemo-naïve patients with stage III or IV PA, age 18-75 yrs, Karnofsky performance status (PS) >50 received P (30 mg/m^2 day 1), G (800 mg/m^2 day 1), X (1250 mg/m^2/day, days 1 to 14) and E at 30 mg/m^2 day 1. Cycles were repeated every 14 days for a maximum of 6 months.

Results. Between June 2006 and December 2010, 125 patients were treated at our institution with the PEXG regimen. Patients' characteristics were: median age 60 years, PS >70 95%, metastatic disease 57%; CA19.9 >upper limit of laboratory normal (ULN) 87%, median CA 19.9 307 UI/mL. PFS6 for stage III patients was 81% and median PFS 10.0 months. In stage IV patients PFS6 was 44% and median PFS 5.8 months. One-year OS for stage III patients was 73% with a median OS of 19.5 months; in stage IV patients 1-y OS was 46% and median OS was 11.8 months. A partial response was observed in 39% of patients (42% and 38% in stage III and IV, respectively). Altogether, 514 cycles of chemotherapy were administered. Main per cycle G3-4 toxicity was: neutropenia 14%, thrombocytopenia 2%, anemia 4%, fatigue 3%.

Conclusions. The PEXG yielded similar results when compared to prior series treated by PEFG. The present trial confirms the relevant impact of this regimen on the outcome of advanced PA and its feasibility on an outpatient basis. Further investigation of the PEXG regimen also in the peri-operative setting is warranted.

C8 PROGNOSTIC SIGNIFICANCE OF *ERBB2* COPY NUMBER VARIATIONS IN PLASMA OF PATIENTS WITH LOCALLY ADVANCED ESOPHAGEAL CARCINOMA (EC)

De Vita F.[3], Andolfo I.[1,2], Orditura M.[3], Petrosino G.[1], Vecchione L.[3], De Antonellis P.[1], Capasso M.[1], Montanaro D.[1], Gemei M.[1], Troncone G.[1], Iolascon A.[1,2], Ciardiello F.[3], Zollo M.[1,2]

[1]CEINGE, Centro di Ingegneria Genetica e Biotecnologia Avanzate, Naples, Italy; [2]Dipartimento di Biochimica e Biotecnologie Mediche, Università degli Studi di Napoli "Federico II", Naples, Italy; [3]Oncologia Medica, Dipartimento Medico-Chirurgico di Internistica Clinica e Sperimentale "F. Magrassi e A. Lanzara" SUN, Seconda Università degli Studi, Naples, Italy

Background. The role of *erbB2* in EC is controversial. We evaluated the detection of *erbB2* copy number (CN) in the free DNA from plasma of EC patients and correlated their variations to VEGF plasma levels. To verify the source of this DNA in the plasma of patients, we isolated circulating tumor cells (CTCs) and analyzed the *erbB2* CN obtained from them.

Patients and methods. Plasma of 41 patients with locally advanced EC was collected before preoperative chemoradiotherapy. DNA was extracted to analyze copy number variations of the *erbB2* gene using real-time PCR assays. The levels of the VEGF-A in the plasma used for *erbB2* amplifications were determined using a commercially available ELISA kit. The CTCs were selected by a gate based on cytokeratin CK8, CK18 and CK19/CD326 expression and were purified by a BD FACS. Tumor blocks were examined by immunohistochemistry for erbB2 expression.

Results. The real-time PCR for *erbB2* gene showed significant ($p = 0.001$) copy number variations in the plasma of EC patients, as compared to healthy controls with high sensitivity (80%) and specificity (95%). PFS curves for EC patients were divided according to *erbB2* CN ≤2 and *erbB2* CN >2. *ErbB2* CN >2 was significantly correlated to a worse PFS ($p = 0.03$). High plasmatic VEGF levels were significantly correlated to a shorter PFS ($p < 0.00001$). The *erbB2* CN variations did not show any significant association with VEGF levels. However, an *erbB2* CN >2 was associated to a worse PFS in patients with low VEGF levels ($p = 0.05$).The analysis of DNA extracted from the CTCs of the patients showed that the *erbB2* CN was in the same range (CN >2) as for the DNA isolated from the plasma of the same patients. A strong expression of erbB2 was observed in *erbB2* CN >2 patients.

Conclusion. The copy number variation of *erbB2* gene appears as prognostic marker to select EC patients with a worse clinical outcome.

C9 ^{177}LU-DOTATATE PEPTIDE RECEPTOR RADIONUCLIDE THERAPY IN NEUROENDOCRINE TUMOURS (NETS): PRELIMINARY RESULTS IN GASTROENTEROPANCREATIC (GEP) TUMOURS OF A PHASE II TRIAL

Sansovini M.[1], Severi S.[1], Ambrosetti A.[1], Milandri C.[2], Bodei L.[5], Scarpi E.[3], Monti M.[3], Carrara F.[1], Paganelli Giulia[1], Sarnelli A.[4], Paganelli G.[1,5]

[1]Nuclear Medicine Unit, [2]Department of Medical Oncology, [3]Biostatistics and Clinical Trials Unit, [4]Medical Physics Unit, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), Meldola (FC), Italy; [5]Department of Nuclear Medicine, IEO, Milan, Italy

Purpose. Peptide receptor radionuclide therapy with ^{177}Lu-dotatate (Lu-TATE-PRRT) is an useful tool in the treatment of neuroendocrine tumours, showing encouraging objective response rates and low toxicity. Here, we report the results of a phase II trial, started in 2008 at the Cancer Institute of Romagna (IRST), Italy.

Patients and methods. The study comprised two groups of GEP-NETs patients treated with Lu-TATE-PRRT cumulative activities based on the presence or absence of risk factors for renal and bone marrow toxicity such as hypertension, diabetes or previous chemotherapy. The majority of patients were in progression at enrolment. Response rate was assessed by WHO criteria. Patients with risk factors were treated up to a median cumulative dose of 500 mCi (min 300-max 650), while those without risk factors were given 700 mCi (min 450-max 750). Both groups received an average of 5 treatment cycles (min 3-max 5) 6 to 8 weeks apart.

Results. To date, 68 patients with metastatic neuroendocrine GEP-NETs have been evaluated. Of the 35 patients with risk factors, 17% showed an objective response (CR + PR + MR), 66% a disease stabilization (SD), and 17% a disease progression (PD). Of the 33 patients without risk factors, 18% demonstrated an objective response, 64% a SD, and 18% a PD. Median progression-free survival was 30 months and the median duration of response was 17 months. No serious adverse events occurred in either group. Grade 2 and 3 toxicity was reported in 3% and 1% of patients, respectively. Severe toxicity (grade 3) was infrequent and occurred only in the risk factors' group.

Conclusion. Lu-TATE-PPRT proved to be effective and safe, and our results agreed with literature data. Two important findings emerged from this study: 1) the difference, in terms of objective response was not significant between the two cumulative treatment doses; and 2) the toxic effects reported in both patient groups were very low and not dose-dependent.

C10 METRONOMIC CAPECITABINE AS SECOND-LINE TREATMENT AFTER SORAFENIB FOR HEPATOCELLULAR CARCINOMA

de Rosa F.[1], Di Girolamo S.[1], Corbelli J.[1], Longobardi C.[1], Agostini V.[1], Andreone P.[2], Serra C.[3], Piscaglia F.[2], Trevisani F.[2], Golfieri R.[4], Bolondi L.[2], Pinna A.D.[5], Biasco G.[1], Brandi G.[1]

[1]Department of Hematology and Oncological Sciences, University of Bologna, Bologna, Italy; [2]Department of Clinical Medicine, University of Bologna, Bologna, Italy; [3]Liver Transplantation Unit, [4]Radiology Unit, Policlinico Sant'Orsola-Malpighi, Bologna, Italy; [5]Department of General and Transplantation Surgery, University of Bologna, Bologna, Italy

Background. The antiangiogenic drug sorafenib is standard treatment for advanced hepatocellular carcinoma (HCC) patients. On sorafenib failure no therapeutic strategy has proven effective and usually only supportive care is offered. However, other antiangiogenic therapies may be effective as well. Metronomic chemotherapy, i.e. continuous administration of low doses of cytotoxic anticancer drugs, is characterized by very good tolerability and enhanced antiangiogenic activity. Therefore we started a phase II clinical trial in advanced HCC patients.

Methods. This is a phase II, monocentric, open-label clinical trial allowing inclusion of 30 advanced HCC patients. Other main inclusion criteria were Child-Pugh liver function class A,

ECOG performance status 0 or 1, adequate haematological and renal function, written informed consent. Main exclusion criteria were sorafenib treatment within 14 days prior to study entry, known or suspect intolerance or hypersensitivity to fluorouracil or its prodrugs, life expectancy inferior than three months. Treatment schedule was capecitabine 500 mg bid. Primary objective of the study is response rate at three months, evaluated per RECIST 1.1 criteria. Secondary objectives are overall survival, time to progression, and toxicity, evaluated per CTCAE 3.0.

Results. Thirty-one patients were included, 28 are evaluable for progression. We observed no objective responses, 10 stable disease and 18 progressive disease; median time to progression was 3.27 months. All patients are evaluable for survival (median overall survival 9.77 months). Significant prognostic factors for survival were BCLC stage and disease control at three months. In multivariate analysis only disease control at three months was an independent predictor of survival (18.0 months vs 6.63 months, HR 0.26, 95% CI 0.07-0.93, p = 0.039). Thirty patients are evaluable for toxicity. It was generally low, and most adverse events were grade 1-2.

Conclusion. Metronomic capecitabine has clinical activity in advanced HCC patients who have failed sorafenib, with a favourable safety profile. Further evaluations are needed to assess its impact on survival.

C11 ASBESTOS: A PUTATIVE RISK FACTOR FOR INTRAHEPATIC CHOLANGIOCARCINOMA

Mattioli S.[a], Di Girolamo S.[b], Farioli A.[a], de Rosa F.[b], Curti S.[a], Corbelli J.[b], Longobardi C.[b], Agostini V.[b], Garajovà I.[b], Paragona M.[b], Violante F.S.[a], Biasco G.[b], Brandi G.[b]

[a]Section of Occupational Medicine, Department of Internal Medicine, Geriatrics and Nephrology, University of Bologna, Bologna, Italy; [b]Department of Hematology and Oncological Sciences L. e A. Seragnoli, Policlinico Sant'Orsola Malpighi, University of Bologna, Bologna, Italy

Introduction. Cholangiocarcinoma (CC) represents about 15% of primary liver tumours in the world.

In the last thirty-year period, a progressive increase of incidence and mortality for CC has been reported worldwide and it mainly involves the intrahepatic form (ICC).

Some conditions activating chronic inflammatory pathways are well recognised as risk factors but they are responsible for only 10% of CC cases.

Probably other environmental factors are involved in the remaining 80-90% of cases and asbestos could be one of these.

We conducted a case-control analysis to explore the association between occupational exposure to asbestos and CC development.

Methods. This study was based on historical data from 155 consecutive patients affected by histologically confirmed cholangiocarcinoma (69 affected by ICC and 86 by extrahepatic cholangiocarcinoma [ECC]) referring to our institution in 2007-2011.

When feasible, cases were individually matched (ratio up to 1:4) by calendar period of birth (5-year intervals), sex and provenience to historical populations controls (sampled from studies of carpal tunnel syndrome, renal cell carcinoma and retinal detachment).

Occupational exposure to asbestos was assessed by industrial hygienists considering lifetime prevalent job-titles. Separate conditional logistic regression models were conducted for ECC and ICC; estimates were adjusted for smoking status and socioeconomic class.

Results. We matched 149 controls to 49 cases of ICC and 212 controls to 59 cases of ECC. We found an increased risk of ICC in workers exposed to asbestos (adjusted OR 4.73, 95% CI 1.54-14.54); conversely, no evidence of increased risk was found for ECC (adjusted OR 1.84, 95% CI 0.66-5.08). Sensitivity analyses conducted using only patients from our city district (Bologna) (conducted to minimize referral bias) produced confirmatory figures (unadjusted OR of ICC 3.67; unadjusted OR of ECC 1.09).

Conclusions. Findings from our exploratory study support the hypothesis that ICC could arise from chronic inflammation caused by presence of asbestos fibers and the relationship between asbestos exposure and cholangiocarcinoma could partially explicate the worldwide increase in ICC incidence.

C12 EGFR AND DOWNSTREAM SIGNALS IN SMALL BOWEL ADENOCARCINOMA: SIMILARITIES WITH COLORECTAL CANCER?

De Dosso S.[1], Riva A.[2], Trezzi R.[2], Zanellato E.[2], Nucifora M.[2], Molinari F.[2], Martin V.[2], Bordoni A.[3], Movilia A.[4], Boldorini R.[5], Bertolini V.[6], Mazzucchelli L.[2], Saletti P.[1], Frattini M.[2]

[1]Oncology Institute of Southern Switzerland, Bellinzona, Switzerland; [2]Institute of Pathology, Locarno, Switzerland; [3]Ticino Cancer Registry, Locarno, Switzerland; [4]Department of Pathology, Civil Hospital, Legnano, Italy; [5]Department of Medical Sciences, University School of Medicine, Novara, Italy; [6]Department of Pathology, Multimedica, Milan, Italy

Background. Small bowel adenocarcinoma (SBA) is a rare malignancy and exhibits similar pathological patterns as compared with colorectal carcinoma (CRC), leading to the hypothesis that these neoplasms might share a superimposable genetic profile. In CRC, deregulation of EGFR correlates with response to anti-EGFR drugs. Conversely, mutations in K-Ras, BRAF or PIK3CA, and loss of expression of PTEN are associated with drug resistance.

The aim of this study was to characterize the deregulation of the EGFR pathway in SBA, which could potentially provide a rationale for the investigation of anti-EGFR agents, as their role in this condition is as yet unexplored.

Methods. Thirty-nine primary SBA were analyzed. We assessed the EGFR gene status by FISH, the mutational status of K-Ras, BRAF and PIK3CA by direct sequencing, and the protein expression of PTEN by immunohistochemistry.

Results. EGFR gene copy number gain was observed in 19 out of 33 analyzable cases (57.5%). In the entire cohort, K-Ras mutations were detected in 17 patients (43.6%), 16 in codon 12 and 1 in codon 61. BRAF mutations were found in 1 case (2.6%), PIK3CA mutations in 4 (10.2%) and loss of PTEN protein expression in 10 (25.6%). All cases with PIK3CA mutation showed a normal PTEN expression. Only 9 cases (23%) exhibited EGFR gene deregulation and absence of genetic alterations in EGFR-downstream pathways.

Conclusions. The genetic profile of EGFR pathway in SBA appears to be similar to CRC. According to the molecular patterns, EGFR-targeted agents could be considered as a potential option also for selected patients with SBA.

C13 GIDEON (GLOBAL INVESTIGATION OF THERAPEUTIC DECISIONS IN HCC AND OF ITS TREATMENT WITH SORAFENIB) STUDY FIRST INTERIM RESULTS: SORAFENIB DOSING ACROSS REGIONS AND DISEASE SUBGROUPS

Daniele B.[1], Bronowicki J.P.[2], Lencioni R.[3], Venook A.[4], Marrero J.[5], Kudo M.[6], Ye S.L.[7], Nakajima K.[8], Cihon F.[8], Papandreou C.[9]

[1]Oncology Unit, G. Rummo Hospital, Benevento, Italy; [2]University Hospital of Nancy, University Henri Poincaré, Vandœuvre-lès-Nancy, France; [3]Pisa University School of Medicine, Pisa, Italy; [4]University of California, San Francisco, CA; [5]University of Michigan, Ann Arbor, MI, USA; [6]Kinki University School of Medicine, Osaka, Japan; [7]Zhongshan Hospital, Fudan University, Shanghai, China; [8]Bayer HealthCare Pharmaceuticals, Montville, NJ, USA; [9]University Hospital of Larissa, Larissa, Greece

Background. Sorafenib (S) is the first systemic therapy indicated to treat unresectable hepatocellular carcinoma. GIDEON is an ongoing, global, prospective non-interventional study of S in real-life practice. Treatment decisions are made at physicians discretion according to local product information. Characterization of S dosing patterns from the first interim analysis is presented.

Methods. The pre-specified first interim analysis was triggered at ≥4 months follow-up of the initial ~500 treated patients; 479 were valid for safety evaluation. Demographic data, medical/disease history are recorded at entry. S dosing and adverse events (AEs) are collected.

Results. Descriptive subgroup data on S dosing, AEs (including discontinuations) are presented (Tables 1 and 2). The initial S dose was <800 mg/day in ~25% of 479 patients without clinically significant differences in AE incidence by initial dose. S dosing and AEs were similar in older (≥65 years) and younger patients.

Conclusions. Interim GIDEON results suggest that Barcelona Clinic Liver Cancer (BCLC) and Child-Pugh status do not appear to determine starting dose of S. Elderly patients tolerated sorafenib as well as younger patients.

C14 PHASE II STUDY OF DOSE-DENSE CHEMOTHERAPY (CT) WITH MODIFIED DOSE-DENSE TCF REGIMEN (TCF-DD) IN METASTATIC GASTRIC CANCER (MGC)

Tomasello G., Poli R., Dalla Chiesa M., Liguigli W., Lazzarelli S., Brighenti M., Curti A., Passalacqua R.

Azienda Istituti Ospitalieri di Cremona, Cremona, Italy

Background. We previously (ASCO 2010) reported on the promising activity of TCF-dd in MGC. These are the final results of a phase II study (EUDRACT no. 2007-004693-34)

Methods. Patients (pts) with histologically confirmed measurable or evaluable MGC, ECOG PS 0-1, not previously treated for the advanced disease, received docetaxel 70 mg/m^2 day 1, cisplatin 60 mg/m^2 day 1, l-folinic acid 100 mg/m^2 day 1 and 2, followed by 5-fluorouracil 400 mg/m^2 bolus day 1 and 2, and then 600 mg/m^2 as a 22 hour continuous infusion day 1 and 2, every 14 days, plus pegfilgrastim 6 mg on day 3. Patients aged ≥65 years received the same schedule with a dose reduction by 30%.

Results. Study duration: December 2007-November 2010. Forty-six consecutive pts were enrolled (78.3% male, 21.7% female; median age: 66, range 38-76; ECOG PS 0: 48%, 1: 46%, 2: 6%. Primary endpoint was overall response rate (ORR). A median of 4 cycles (range 1-6) was administered. Forty-three pts were evaluated for response (93.5%) and all for toxicity. 3 CR, 25 PR, 10 SD and 5 PD were observed, for an ORR by ITT of 61% (95% CI 47-75). Median overall survival was 17.63 months (95% CI 13.67-20.67); median TTP was 10.67 (95% CI 7.1-14.2) months. Twenty-one pts (46.0%) were treated at full doses without any delay thus respecting the dose-dense criterion. Most frequent grade 3-4 toxicities were: neutropenia (20%), leucopenia (4.3%), thrombocytopenia (2.2%), anemia (2.2.%), febrile neutropenia (6.5%), asthenia (22%), diarrhea (4.3%), nausea/vomiting (11%) and hypokalemia (6.5%). Overall TCF-dd was shown to be safe.

Conclusions. TCF-dd regimen in MGC confirms to be feasible and very active and needs to be tested in randomized studies.

Table 1 - C13

Adverse events by age and starting dose subgroups	<65 years No. (%) 286	≥65 years No. (%) 193	Starting dose 400 mg/day No. (%) 104	Starting dose 800 mg/day No. (%) 363	Total No. (%) 479
AE (all grades) - any/drug related	246 (86)/188 (66)	169 (88)/131 (68)	100 (96)/77 (74)	308 (85)/238 (66)	415 (87)/319 (67)
Serious AE (all grades) - any/drug related	124 (43)/31 (11)	77 (40)/20 (10)	49 (47)/11 (11)	151 (42)/39 (11)	201 (42)/51 (11)

Table 2 - C13

Sorafenib (S) dosing and discontinuation due to AEs by disease subgroups and age	BCLC				Child-Pugh status		Age (years)		Total
	A No. 47	B No. 92	C No. 253	D No. 29	CP-A No. 278	CP-B No. 134	<65 No. 286	≥65 No. 193	No. 479
Initial dose 800 mg/day, no. (%)	33 (70.2)	72 (78.3)	200 (79.1)	24 (82.8)	221 (79.5)	100 (74.6)	219 (76.6)	144 (74.6)	363 (75.8)
Permanent discontinuation of S due to AEs, no. (%)	12 (25.5)	20 (21.7)	71 (28.1)	11 (37.9)	69 (24.8)	53 (39.6)	74 (25.9)	59 (30.6)	133 (27.8)

C15 CIRCULATING METALLOPROTEINASE-3 AND TISSUE INHIBITOR OF METALLOPROTEINASE-2 IN PATIENTS WITH DUCTAL PANCREATIC NEOPLASMS

Vecchiarelli S.[a], Macchini M.[a], Di Marco M.[a], Pezzilli R.[b], Fabbri D.[b], Imbrogno A.[b], Casadei R.[c], Melzi d'Eril G.[d], Sina S.[a], Biasco G.[a]

[a]Department of Hematology and Oncological Sciences "L. e A. Seràgnoli", Sant'Orsola-Malpighi Hospital, Bologna;, [b]Department of Digestive Diseases and Internal Medicine, Sant'Orsola-Malpighi Hospital, Bologna; [c]Department of Emergency, General and Transplant Surgery, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna; [d]Department of Medicine, Surgery and Dentistry, University of Milan, Milan, Italy

Introduction. There is increasing evidence regarding the involvement of inflammation in patients with intraductal papillary mucinous neoplasms (IPMNs) of the pancreas.

Objectives. To evaluate the circulating concentrations of MMP-3 and TIMP-2 in patients with IPMNs and in those with ductal adenocarcinomas (ADAC).

Patients. Sixty patients (32 males, 28 females, mean age 69.3±11.3 years) were enrolled: 31 (51.7%) had IPMNs and 29 (48.3%) had histologically confirmed ADAC. Thirty blood donors were also studied as controls.

Materials and methods. The serum concentrations of MMP-3 and TIMP-2 were determined in all study subjects using commercially available kits.

Results. Serum concentrations of MMP-3 were significantly higher both in patients with ADAC (14.8 ± 11.3 ng/mL) and in those with IPMNs (18.2 ± 19.8 ng/mL) as compared to the healthy subjects (5.9 ± 2.9 ng/mL, $p = 0.001$) whereas serum levels of TIMP-2 were significantly lower both in IPMN patients (91.3 ± 23.5 ng/mL) and in patients with ADAC (84.7 ± 18.2 ng/mL) than in those of the healthy subjects (141.3 ± 47.9 ng/mL, $p < 0.001$). No significant differences in the serum levels of both MMP-3 and TIMP-2 were found between patients with IPMNs and those with ADAC as well as in the patients with branch type IPMN (MMP-3: 20.0 ± 16.5 ng/mL; TIMP-2: 94.7 ± 24.4 ng/mL) as compared to those with main duct IPMN (MMP-3: 16.2±23.3 ng/mL, $p = 0.220$; TIMP-2: 87.7 ± 22.7 ng/mL, $p = 0.607$).

Conclusions. IPMNs have a pattern of extracellular matrix factors and their inhibitors are similar to those of ADAC; MMP-3 and TIMP-2 cannot be utilized to routinely differentiate IPMNs from ductal adenocarcinomas.

C16 CLINICOPATHOLOGICAL FACTORS INFLUENCING PROGNOSIS IN EARLY GASTRIC CANCER PATIENTS UNDERGOING RADICAL SURGICAL RESECTION

Galizia E.[1], Scartozzi M.[2], Mari D.[1], Giampieri R.[2], Pistelli M.[2], Bittoni A.[2], Di Pietro Paolo M.[1], Salvucci G.[1], Safi M.[1], Mulattieri S.[1], Giuliodori L.[1], Berardi R.[2], Cascinu S.[2], Silva R.R.[1]

[1]U.O. Oncologia, Ospedale "E. Profili", Fabriano; [2]Clinica Oncologia Medica, Ospedali Riuniti, Ancona

Background. Early gastric cancer (EGC) is defined as a lesion in which the depth of invasion is limited to the mucosa, submucosa or both, regardless of lymph node status. Despite an appropriate surgical treatment, about 10-15% of all patients diagnosed with EGC will eventually relapse. Clinical prognostic factors able to identify those cases more likely to recur are lacking and may be crucial to determine post-surgical management in these patients.

Aim. Aim of our analysis was to identify putative prognostic factors in a group of radically resected EGC cancer patients.

Patients and methods. Patients population was selected from a central database including 1065 patients with gastric cancer, operated in four different Institutions.

Clinicopathological characteristics and prognostic outcomes of 202 patients undergoing a radical surgical resection for EGC between 1977 and 2008 were retrospectively evaluated. Multiple factors were analysed, including age at diagnosis, sex, tumour histology, lymphatic/blood vessel invasion (LBVI), type of lymphadenectomy, lymph nodes status and tumour grading.

Results. At univariate analysis, the presence of LBVI, lymph nodes metastases and a limited lymphadenectomy showed a significant effect on predicting a poor prognosis, both for overall (OS) and disease-free survival (DFS).

The multivariate analysis identified LBVI and lymph nodes metastases as independent prognostic factors for OS and DFS ($p = 0.0008$ and $p = 0.0001$ respectively) in EGC patients.

Conclusions. EGC patients with lymph nodes involvement and LBVI are at higher risk of recurrence and surgical outcome in this population is relatively poor.

These results suggest that an adequate classification of EGC should always include an adequate lymph nodes clearance. On the other hand LBVI proved to be a further prominent factor influencing outcome in these patients.

As a consequence for post-surgical management, an intensive follow-up may be a more appropriate choice for patients showing either lymph nodes involvement or LBVI or both.

C17 DNA POLYMORPHISMS AND CLINICAL OUTCOME IN BILIARY TRACT CANCER PATIENTS TREATED WITH EPIRUBICIN, CISPLATIN AND CAPECITABINE (ECX) REGIMEN

Mambrini A.[1], Giovannetti E.[2], Pacetti P.[1], Zaccarelli E.[2], Orlandi M.[1], Alecci C.[2], Pezzuolo D.[1], Giancola F.[2], Peters G.J.[2], Cantore M.[1]

[1]Department of Medical Oncology, Carrara Hospital, Italy; [2]Department of Medical Oncology, VUmc, Vu University Medical Center, Amsterdam, The Netherlands

Background. Biliary tract cancers (BTC) are rare tumours with a few therapeutic options. Our previous phase II study showed that combined locoregional and systemic chemotherapeutic regimen was active and safe, with results similar to the gemcitabine-platinum regimen (Cantore et al., Cancer, 2005; Valle et al., N Engl J Med, 2010). The identification of predictive factors of drug activity is crucial for maximizing therapeutic efficacy. Therefore this study was aimed at evaluating the association of polymorphisms in key genes with outcome of BTC patients (pts) treated with intraarterial cisplatin and epirubicin, and oral capecitabine (ECX) regimen.

Patients and methods. We evaluated 5 polymorphisms in 4 genes (ERCC1, XPD, XRCC1 and TS) in 75 unresectable BTC

pts treated upfront with ECX. Univariate/multivariate analyses compared clinical (age, sex, performance status (PS), CA19.9, cycle numbers) and genetic parameters with clinical response, overall and progression-free survival (OS, PFS).

Results. Patients harbouring a higher number of repeats in the TS promoter enhancer region (e.g., TSER 3R3R or 2R3R) experienced a significantly lower rate of clinical benefit (54 vs 80%, p = 0.03) and shorter OS (p = 0.001, with median OS of 6.7, 9.0 and 19.3 months in pts with TSER 3R3R, 2R3R and 2R2R genotypes, respectively). CA19.9 levels above 100 U/mL were also associated with lower rate of clinical response and shorter OS, while no correlations were observed for all the other parameters. TSER polymorphic variants and CA19.9 remained as independent predictors for death risk at Cox multivariate analysis.

Conclusions. TSER polymorphisms have been already associated with differential outcome in cancer pts treated with fluoropyrimidine based regimens, but this is the first evidence about their predictive role in BTC pts treated with ECX regimen. Since BTC are such a dismal disease, any biomarker that can help to better stratify patients might have crucial clinical applications. The validation of the role of these polymorphisms in future prospective studies will offer new tools for optimization of currently available treatments in selected patients.

C18 FOLFIRI AS SALVAGE THERAPY AFTER FLUOROPYRIMIDINE AND PLATINUM-BASED FIRST-LINE CHEMOTHERAPY FOR ADVANCED GASTRIC CANCER: MULTIVARIATE ANALYSIS OF PROGNOSTIC FACTORS

Giordani P.[1], Catalano V.[1], Santini D.[2], Spada D.[3], Bisonni R.[4], Vasile E.[5], Alessandroni P.[1], D'Emidio S.[1], Vincenzi B.[2], Baldelli A.M.[1], Rossi D.[1], Testa E.[3], Giustini L.[4], Falcone A.[5], Tonini G.[2], Graziano F.[1]

[1]U.O.C. Oncologia, A.O. "Ospedale Riuniti Marche Nord", Presidio San Salvatore, Pesaro, Italy; [2]Oncologia, Università Campus BioMedico, Rome, Italy; [3]Oncologia, Ospedale di Urbino, Urbino, Italy; [4]Oncologia, Ospedale "A. Murri", Fermo, Italy; [5]Oncologia 2 Universitaria, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy

Background. First-line chemotherapy containing fluoropyrimidine and platinum is generally considered standard for patients (pts) with advanced gastric cancer (AGC). Second-line chemotherapy with irinotecan was shown to improve overall survival (OS) compared with best supportive care (Thuss-Patience et al., Proc ASCO 2009:#4540) and FOLFIRI is one of the most used regimens as salvage therapy. The aim of this retrospective analysis was to assess the influence of clinico-pathologic factors on the survival of AGC patients receiving FOLFIRI as second-line chemotherapy at five oncology departments.

Method. One hundred patients with AGC progressing to previous first-line regimens containing fluoropyrimidines (5-FU or capecitabine) and platinum analogues (cisplatin or oxaliplatin) were eligible for the study. Patients received irinotecan 180 mg/m^2 day 1 followed by leucovorin 100 mg/m^2 plus 5-FU 400 mg/m^2 bolus and 600 mg/m^2 in a 22-h infusion, on days 1 and 2 (FOLFIRI) or by leucovorin 200 mg/m^2 plus 5-FU 400 mg/m^2 bolus and 5-FU 2,400 mg/m^2 in a 46-h continuous infusion (simplified FOLFIRI), every 2 weeks. Treatment was continued until progression of disease or unacceptable toxicity.

Results. Median age of patients was 68 years (range 33-85 years), M/F 69/31, ECOG performance status 0/1/2/3 in 22/50/26/2 pts. The predominant metastatic sites were lymph nodes (48 pts), peritoneum (48 pts), liver (33 pts), and 70% of pts had 2 or more sites of disease. The median number of cycles was 6 (range 1-18) and 34 pts received simplified FOLFIRI. One patient and 14 pts achieved complete and partial response, respectively, with an overall response rate of 15% (95% CI 8-22). After a median follow-up of 36 months, median progression-free survival and OS were 3.5 months (95% CI, 3.2-3.9) and 7.9 months (95% CI, 7.1-8.9), respectively, with 1-year OS of 28.1%. In multivariate analysis using the Cox proportional hazards model, age ≥65 years (hazard ratio, HR = 1.83; 95% CI, 1.15-2.91; p = 0.011) and ECOG performance status 2-3 (HR = 2.01; 95% CI, 1.15-3.53; p = 0.014) were the two variables independently associated with poor overall survival.

Conclusions. FOLFIRI showed a moderate activity as salvage therapy in AGC pts progressing to first-line fluoropyrimidine/platinum-based chemotherapy. However, some easily available clinical factors, such as performance status and age, may help to select the groups of patients with AGC more likely to benefit from FOLFIRI as salvage therapy.

C19 SORAFENIB TREATMENT AND SAFETY PROFILE IN CHILD PUGH B PATIENTS CHARACTERIZED IN FIRST INTERIM RESULTS OF GIDEON (GLOBAL INVESTIGATION OF THERAPEUTIC DECISIONS IN HEPATOCELLULAR CARCINOMA AND OF ITS TREATMENT WITH SORAFENIB)

Lencioni R.[1], Daniele B.[2], Marrero J.[3], Lim H.Y.[4], Stål P.[5], Kudo M.[6], Venook A.[7], Nakajima K.[8], Ye S.L.[9]

[1]Division of Diagnostic Imaging and Intervention, Department of Liver Transplantation, Hepatology and Infectious Diseases, Pisa University School of Medicine, Pisa, Italy; [2]Oncology Unit, G. Rummo Hospital, Benevento, Italy; [3]Department of Internal Medicine, Division of Gastroenterology, University of Michigan, Ann Arbor, MI, United States; [4]Samsung Medical Center, Seoul, Korea; [5]Department of Gastroenterology, Karolinska University Hospital/Huddinge, Stockholm, Sweden; [6]Department of Gastroenterology and Hepatology, Kinki University School of Medicine, Osaka, Japan; [7]University of California, San Francisco, USA; [8]Global Medical Affairs, Bayer HealthCare Pharmaceuticals, Montville, NJ, USA; [9]Liver Cancer Institute, Zhongshan Hospital, Fudan University, Shanghai, China

Aim. The aim of GIDEON, the largest ongoing, global, prospective, non-interventional study of patients (pts) with unresectable HCC (uHCC) eligible for systemic therapy and receiving sorafenib (S), is to evaluate S safety and efficacy in diverse real-life clinical settings and pt subgroups, e.g., Child-Pugh (CP) B.

Methods. Demographic data, medical, disease and treatment history were recorded. At follow-up visits S dose, concomitant treatments, performance status, liver function, adverse events (AEs) and efficacy, assessed per Response Evaluation Criteria in Solid Tumors, were recorded. Target accrual was 3000 pts from >40 countries. Per protocol, the first interim analysis was triggered when 500 enrolled pts were followed over a minimum of 4 mos.

Results. In total, 479 patients were eligible for analysis [CP A (n = 278, 58%) and B (n = 134, 28%) pts; 11 (2%) pts were CP C and 56 (12%) pts did not have evaluable data]. S starting dose

was 800 mg in the largest percentage of pts in the CP A (80%) and B (75%) groups, with no dose interruptions in 73% and 78% and no dose modifications in 55% and 63% of the CP A and B groups respectively. BCLC (Barcelona-Clinic Liver Cancer) stage C and TNM (Tumour, Node, Metastasis) stage IV were the most prevalent stages in CP A, 54% and 37% respectively, and in CP B, 53% and 31%. The most common previous treatment for HCC was TACE (transarterial chemoembolization) in both CP A (48%) and CP B (38%) pts. S afety profile was comparable in the CP A and B groups, with the exception that a greater percentage of CP B pts (40% vs 25%) discontinued S therapy due to AEs.

Conclusion. GIDEON is collecting important data on CP B pts treated with S, and to date while there were more on-treatment AEs and deaths within the CP B group, we believe these represent the natural history of the liver disease as opposed to a drug effect.

C20 OUTCOME OF LOCALLY ADVANCED GASTRO-ESOPHAGEAL JUNCTION (GEJ) AND GASTRIC CANCER: OPTIMAL LYMPHADENECTOMY FIRST OF ALL. A SINGLE-INSTITUTION ANALYSIS

Catalano V.[1], Sisti V.[2], Graziano F.[1], Spada D.[3], Cicetti M.[2], Giordani P.[1], Alessandroni P.[1], D'Emidio S.[1], De Nictolis M.[4], Testa E.[3], Zingaretti C.[2]

[1]U.O.C. Oncologia, [2]U.O.C Chirurgia Generale, Oncologica e Vascolare, Azienda Ospedaliera "Ospedali Riuniti Marche Nord", Presidio San Salvatore, Pesaro; [3]U.O.C. Oncologia, Ospedale di Urbino, Urbino; [4]U.O.C. Anatomia Patologica e Citologia, Azienda Ospedaliera "Ospedali Riuniti Marche Nord", Pesaro, Italy

Background. Complete surgical resection (R0) of the primary tumour and regional lymphadenectomy is the treatment of choice for gastric cancer. Perioperative chemotherapy is considered a standard approach for locally advanced (LA) gastric and GEJ cancer. In the present study we examined morbidity, mortality, and outcomes for patients treated with total gastrectomy (TG) plus at least D2 lymphadenectomy for operable LA GEJ and gastric cancer.

Methods. From January 1998 to February 2009, 245 patients with LA adenocarcinoma (pT2N+, pT3-4Nx; AJCC 7th edition) received primary curative intent resection at San Salvatore Hospital. Surgical treatment for any primary site of disease was TG associated with D2 lymphadenectomy extended to the 3rd level 12p/b nodes (D2/D3). Progression-free survival (PFS) was calculated from the date of surgery to the first event (i.e., progression or death from any cause), and overall survival (OS) was calculated from the date of surgery to death from any cause.

Results. 145 (59%) patients were male, median age was 73 years (range 36-100), 45 patients (18%) had GEJ/cardia tumours and 16 patients (6%) had gastric stump adenocarcinoma. According to Lauren's classification, 93 patients (38%) showed diffuse type and 24 patients (10%) mixed type tumours. One hundred and five patients (43%) had stage II disease. Median number of examined lymph nodes was 34 (range 4-80), 10 (4%) patients had less than 15 examined lymph nodes. Only 3 patients received perioperative/neoadjuvant chemotherapy, whereas 75 patients (31%) received adjuvant chemotherapy. Major non-fatal complications and mortality rates were 6.1% and 2.8%, respectively. After a median follow-up of 80 months, the 5-year PFS and OS for the entire population was 52.1% and 56.3% (intention-to-treat, ITT). An exploratory analysis was performed for patients aged 75 years or less (n = 148), who are commonly considered candidate for perioperative treatments. This population showed a 5-year PFS and OS of 59.3% and 63.7% (ITT), respectively.

Conclusions. This single-institution experience confirms that D2 lymphadenectomy could be safely performed in high-volume centers and may offer good results in terms of survival rates, also without perioperative treatments. For LA GEJ and gastric cancer, the role of perioperative chemotherapy should be better weighted in patients treated with optimal lymphadenectomy.

C21 THE ROLE OF LDH SERUM LEVELS IN PREDICTING GLOBAL OUTCOME IN HCC PATIENTS UNDERGOING TACE: IMPLICATIONS FOR CLINICAL MANAGEMENT

Faloppi L.[1], Scartozzi M.[2], Bianconi M.[1], Giampieri R.[1], Maccaroni E.[1], Pistelli M.[1], Chiorrini S.[1], Del Prete M.[2], Pierantoni C.[2], Berardi R.[2], Svegliati Baroni G.[3], Cascinu S.[2]

[1]Scuola di Specializzazione in Oncologia Medica, Clinica di Oncologia Medica, Università Politecnica delle Marche, Ancona, Italy; [2]Clinica di Oncologia Medica, [3]Clinica di Gastroenterologia, Azienda Ospedaliero-Universitaria "Ospedali Riuniti Umberto I-Lancisi-Salesi", Università Politecnica delle Marche, Ancona, Italy

Preclinical data suggested that molecular mechanisms underlying tumour angiogenesis and hypoxia may be relevant for the global outcome of patients with hepatocellular carcinoma (HCC).

In many tumour types serum LDH levels proved to represent an indirect marker of tumour hypoxia and worse prognosis. Moreover data about HCC are lacking in particular in the clinical setting of patients undergoing trans arterial-chemoembolization (TACE) in whom hypoxia and neo-angiogenesis may represent the molecular key to treatment failure.

Aim of our analysis was to evaluate the potential prognostic role of lactate dehydrogenase (LDH) in patients treated with TACE.

We retrospectively assessed 114 patients treated with TACE or precision-TACE (Lipiodol or drug eluting microspheres) at our institution. For all patients LDH values were collected within one month before the procedure. Patients response to treatment was evaluated according to new RECIST criteria (1.1). We divided our patients into two groups according to serum LDH levels (group A LDH ≤450U/L: 84 patients; group B LDH >450U/L: 30 patients).

A statistically significant difference ($p = 0.03$) was found in time to progression (TTP) in patients with LDH values under or above the cut-off (group A: median TTP 16.3 months; group B: median TTP 10.8 months). This difference proved to be significant also for overall survival (OS) ($p = 0.024$; group A: median OS 22.4 months; group B: median OS 12.8 months).

The two patients groups proved homogeneous in gender, age, etiology of the cirrhosis, performance status (ECOG), staging systems (Child-Pugh, BCLC, Okuda, MELD and MELD-Na), objective response, administered drug (epirubicin, doxorubicin), TACE technique (TACE or pTACE; Lipiodol or drug eluting microspheres).

In our experience, LDH seemed able to reliably predict outcome in terms of TTP and OS for HCC patients undergoing TACE. According to our findings we could speculate that HCC patients candidate to TACE with high LDH serum levels should receive a more aggressive treatment. This group of patients may

then benefit from a multimodality treatment approach including TACE and anti-VEGF inhibitors in order to decrease the progression rate and improve TTP and OS.

C22 CLINICAL SAFETY AND EFFICACY OF ADJUVANT CHEMOTHERAPY IN RADICALLY RESECTED CHOLANGIOCARCINOMA PATIENTS

Di Girolamo S.[1], de Rosa F.[1], Derenzini E.[1], Frega G.[1], Barbera M.A.[1], Ercolani G.[2], Pinna A.D.[2], Biasco G.[1], Brandi G.[1]

[1]Department of Hematology and Oncological Sciences "Lorenzo e Ariosto Seràgnoli", University of Bologna, Bologna, Italy; [2]Department of General Surgery and Organ Transplantation, University of Bologna, Bologna, Italy

Background. Biliary tract cancer represents about 3% of gastrointestinal malignancies. Surgery is the only therapeutic approach able to achieve long-term disease-free survival. The inadequate results of surgery prompted evaluation of adjuvant treatments. Our study is aimed at evaluating efficacy and toxicity of this approach.

Methods. This is a retrospective analysis on all consecutive patients who underwent surgery for biliary tract cancer in our institution between March 2001 and April 2008.

All radically resected patients were offered adjuvant therapy with gemcitabine 1000 mg/m^2 on days 1, 8, 15 of a 28 days cycle for six cycles. Those who refused chemotherapy entered in a follow-up program.

Patients' characteristics have been compared by Pearson's chi-square test. Disease staging and toxicity have been assessed respectively according to TNM system and NCI-CTCAE 3.0. Survival has been estimated by Kaplan-Meier method. Multivariate analysis on prognostic significant factors in univariate analysis (log-rank test) has been performed according to Cox proportional hazard model.

Results. Of 144 patients, 80 accepted adjuvant therapy and 64 were followed up. Patients' characteristics are not significantly different in the two groups, according to Pearson's chi-square test.

After a median follow-up of 20.5 months, median time to relapse is 18 months in treatment group and 11 months in control group ($p = 0.03$).

Adjuvant therapy is associated with an absolute reduction in relapse risk at 5 years of 6.7%.

In treatment group about two thirds of patients experienced a grade 3/4 toxicity.

No treatment-related deaths occurred, and no patient discontinued treatment because of toxicity.

At univariate analysis, beside adjuvant therapy, intrahepatic cholangiocarcinoma, negative lymph nodes and radical surgery were positive prognostic factors.

In multivariate analysis all these factors maintained statistical significance.

Adjuvant treatment was statistically significant too ($p = 0.0339$).

Conclusions. Adjuvant chemotherapy could represent an interesting option to reduce relapse risk in biliary tract cancer.

A randomized controlled study is required to confirm these data.

C23 SIGNIFICANCE OF BAX AND P53 FOR OUTCOME PREDICTION IN METASTATIC GASTRIC CANCER (mGC) PATIENTS TREATED WITH FIRST-LINE COI (CAPECITABINE, OXALIPLATIN AND IRINOTECAN) REGIMEN

Di Bartolomeo M.[1], Pietrantonio F.[1], Biondani P.[1], Pellegrinelli A.[2], Bianchini G.[1], Colonna V.[1], Dotti K.F.[1], Franceschelli L.E.[1], Buzzoni R.[1]

[1]Department of Medical Oncology, [2]Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Background. Bax plays a central role in apoptosis signalling and might be a chemosensitivity biomarker. P53 is a gene regulator of Bax, but its significativity as independent biomarker is controversial. The aim of this retrospective study was to investigate the predictive/prognostic value of Bax/p53 in mGC pts homogeneously treated with a triplet combination chemotherapy.

Methods. First-line treatment with COI (capecitabine 1000 mg/m^2 twice daily d2-6; oxaliplatin 85 mg/m^2 d2; irinotecan 180 mg/m^2 d1; biweekly schedule) was administered to a consecutive series of mGC pts for up to 8 cycles. Performance status (PS-ECOG) ≤1. Tissue blocks available for 23 pts who provided written consent. Bax/p53 expression assessed by immunohistochemistry, with dicotomic discrimination. Association of both biomarkers with RECIST response by two tailed Fisher's exact test. Correlation of Bax/p53 and PS with progression-free (PFS) and overall (OS) survival by univariate and multivariate Cox's proportional hazard model.

Results. Two patients not evaluable by RECIST criteria. Bax-positive 74% (17/23), negative 26% (6/23); p53 overexpressed 39% (9/23), negative 61% (14/23). Response rate: overall, 71% (15/21, 11 PR/4 CR); Bax-positive, 87% (13/15); Bax-negative 33% (2/6); $p = 0.03$. By Cox univariate analysis, Bax negative tumours had significantly shorter PFS (3.9 vs 7.4 mos; HR = 3.40, 95% CI 1.17-9.93; $p = 0.02$) and OS ($p = 0.04$). In multivariate analysis for Bax and PS, Bax-negative tumours showed a significantly higher risk for progression (HR 4.51, 95% CI 1.30-15.6; $p = 0.02$) and death (HR 6.69, 95% CI 1.30-15.6; $p = 0.01$); suboptimal PS (ECOG 1) was associated with a trend for worst overall survival ($p = 0.08$). p53 evaluation failed to show any significant correlation with outcome.

Conclusions. In mGC pts selected for good-intermediate PS, Bax expression is associated with higher responses to first-line triplet COI regimen. Bax negative tumours showed poorer outcome in terms of PFS and OS, while p53 overexpression did not have an impact on disease prognosis. Prospective confirmation of predictive/prognostic role of Bax in mGC treated with specific chemotherapeutic drugs is warranted.

C24 SECOND-LINE CHEMOTHERAPY IN BILIARY TRACT CANCER PATIENTS

Corbelli J.[1], Di Girolamo S.[1], de Rosa F.[1], Agostini V.[1], Garajová I.[1], Longobardi C.[1], Paragona M.[1], Ercolani G.[2], Pinna A.D.[2], Biasco G.[1], Brandi G.[1]

[1]Department of Hematology and Oncological Sciences "L.A. Seragnoli", Hospital Sant'Orsola-Malpighi, University of Bologna, Bologna, Italy; [2]Department of Surgery and Transplantation, Ho-

spital Sant'Orsola-Malpighi, University of Bologna, Bologna, Italy

Background. Biliary tract cancers are rare malignancies with a very poor prognosis.

Several studies comparing chemotherapy and supportive care showed significant survival prolongation and improvement in the quality of life with chemotherapy.

The association of gemcitabine and a platinum compound is considered the standard first-line treatment but there are no adequate data supporting any second-line therapy.

Our retrospective study aims at evaluating the impact of second-line chemotherapy in this setting.

Methods. We reviewed medical records of patients (pts) affected by histologically confirmed biliary tract cancer, treated in our institution from 2005 to 2010 with a second-line chemotherapy after first-line treatment progression.

Results. We identified 121 pts progressing after first-line chemotherapy. Fifty-six (46%) of these were considered fit for a second-line treatment and 49 (40%) were effectively treated.

Of these 49, 34 had relapsed after radical surgery and 15 were unresectable at diagnosis.

The primary site was intrahepatic in 25 pts, extrahepatic in 18 and gallbladder in 6.

The first-line schedules were mainly gemcitabine plus a platinum compound (n = 35) or gemcitabine plus capecitabine (n = 8).

As second-line, gemcitabine plus a platinum compound and gemcitabine plus capecitabine were delivered respectively in 15 and 14 pts. The remaining 20 were treated with other regimens (6 gemcitabine plus irinotecan, 14 monochemotherapy).

Median time to progression was 3.5 months (95% CI 2.0-5.0) and median overall survival, calculated from the start of second-line treatment, was 8.1 months (95% CI 4.3-11.9).

The median overall survival calculated from the start of first-line was 18.7 months (95% CI 13.9-23.5).

Conclusions. Many patients affected by biliary tract cancer still have a good performance status after first-line chemotherapy and could be treated in second-line with potential survival benefit.

The optimal regimen has not yet been identified.

C25 CLINICAL IMPACT OF T REGULATORY CELLS AND THE CYTOKINE NETWORK REGULATING THEIR ACTIVITIES IN PANCREATIC ADENOCARCINOMA

Vizio B.[1], Novarino A.[2], Cristiano C.[2], Giacobino A.[2], Prati A.[1], Ciuffreda L.[2], Bellone G.[1]

[1]Department of Clinical Physiopathology, University of Turin, [2]Deparment of Medical Oncology, Azienda Ospedaliera Universitaria San Giovanni Battista, Molinette, Turin, Italy

Purpose. $CD4^+CD25^+FoxP3^+$ regulatory T cells (Treg) are understood to maintain peripheral tolerance to self-antigens and inhibit anti-tumour immune responses. However, compelling evidence suggests that, in the tumour microenvironment, Treg provides no antiinflammatory protection, rather contributing to a T helper (h)17-driven procarcinogenic process.

Experimental design. We evaluated by three-color flow cytometry the frequency of circulating $CD4^+CD25^+FoxP3^+$ Treg in the peripheral blood of pancreatic carcinoma patients before and after chemotherapy [gemcitabine (GEM) alone, or GEM + oxaliplatin (OX) or bevacizumab + capecitabine + radiotherapy (BEV + CAPE + RT)]. Correlations were sought between Treg counts and plasma levels of cytokines relevant to controlling Treg/Th17 balance, i.e. IL-23, IL-17A, IL-6 and TGF-β1, measured by ELISA, and pancreatic-cancer clinical features.

Results. Treg, IL-6 and TGF-β1 levels were significantly higher in locally advanced and metastatic patients than controls. None of the parameters were correlated with disease stage except IL-6; IL-17A and TGF-β1 levels were inversely correlated with overall survival. IL-17A levels were positively correlated with those of IL-23. After the treatment course, Treg, IL-6 and TGF-β1 were down after GEM monochemotherapy, IL-23 and IL-17A after GEMOX, and IL-6 after BEV+CAPE+RT. IL-23, IL-7A and TGF-β1 levels were significantly lower in responder patients (partial remission/stable disease) in comparison with those of non-responders (progressive disease).

Conclusions. Our results point to a new perspective concerning the impact of Treg/Th17-balance in pancreatic carcinoma, highlighting the significance of TGF-β1 and IL-17A as potential prognostic and predictive indicators. Immunological changes induced by mono and/or combined chemotherapies indicate specific windows of opportunity for introducing an integrative intervention on new target in pancreatic cancer, i.e. IL-17A, possibly improving survival in this highly lethal disease.

C26 HEPATIC INTRA-ARTERIAL CETUXIMAB, 5-FLUOROURACIL AND CISPLATIN FOR PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA (HCC) NOT RESPONSIVE AND/OR NOT ELIGIBLE FOR SORAFENIB: PRELIMINARY RESULTS ON TWELVE PATIENTS

Poggi G.[1], Montagna B.[1], Melchiorre F.[2], Quaretti P.[3], Delmonte A.[4], Riccardi A.[5], Tagliaferri B.[1], Sottotetti F.[1], Di Cesare P.[1], Pozzi E.[1], Stella G.[6], Villani L.[7], Cornalba G.[2], Bernardo G.[1]

[1]Division of Medical Oncology II, IRCCS S. Maugeri Foundation, Pavia, Italy; [2]Department of Interventional Radiology, S. Paolo Hospital, Milano, Italy; [3]Department of Interventional Radiology, IRCCS S. Matteo Hospital, Pavia, Italy; [4]Medical Oncology, European Institute of Oncology, Milan, Italy; [5]University of Pavia, Pavia, Italy; [6]Dision of Respiratory Disease, IRCCS S. Matteo Hospital, Pavia, Italy; [7]Division of Pathology, IRCCS S. Maugeri Foundation, Pavia, Italy

Background. Sorafenib is the only therapy approved for advanced hepatocellular carcinoma (HCC) no longer eligible to transcatheter arterial chemoembolization. Also hepatic arterial chemotherapy (HAIC) has shown to be an effective and safe therapeutic modality for advanced HCC.

Cetuximab, the anti-EGFR monoclonal antibody approved for the treatment of colorectal and head and neck cancer, has been administered intravenously in patients with advanced HCC, showing encouraging results in terms of safety and toxicity profile.

Our purpose was to evaluate the safety and feasibility of HAIC with cetuximab, cisplatin and 5-FU in patients with advanced HCC, not responsive or not eligible to sorafenib.

Patients and methods. From January 2010 to January 2011 twelve patients received repeated hepatic arterial infusion of chemotherapeutic agents via an injection port implanted. A 2 days course of chemotherapy consisting of daily administration

of cisplatin 20 mg as 2-h infusion, 5-fluorouracil 500 mg/m^2 as 5-h infusion and cetuximab 500 mg/m^2 as 12-h infusion, was administered every 14 days. All enrolled patients had a multinodular hepatic disease, without extrahepatic metastases and with portal tumour invasion in 8 out of 12 cases. Liver functional reserve, evaluated using the Child-Pugh classification, corresponded to grade A score 5 in six patients, grade A score 6 in two and grade B score 7 in four patients. Tumour stage was determined by BCLC and CLIP classifications.

Results. After a mean of four months of therapy, contrast-enhanced CT revealed five partial response, five stable disease and two progressive disease. The toxicity profile was favourable, with no G4 gastrointestinal, hematologic or skin side effects, or severe deterioration of liver function. In the group of four patients treated with more than 12 cycles of chemotherapy, we observed a long maintenance of the tumour response, ranging from 9 to 15 months (mean 12 months).

Conclusion. HAIC with cetuximab is a safe and feasible treatment for advanced HCC, with significant and promising results in a very poor prognosis setting of patients.

C27 COMBINED TREATMENT OF GEMCITABINE (G) PLUS OXALIPLATIN (O) (GEMOX) FOLLOWED BY CHEMORADIOTHERAPY (CT-RT) IN THE TREATMENT OF LOCALLY ADVANCED NON-METASTATIC UNRESECTABLE PANCREATIC CANCER: RESULTS OF A SINGLE INSTITUTE EXPERIENCE PHASE II TRIAL

Torrisi E.°, Buonadonna A.°, Boz G.*, Miolo G.°, Turchet E.^, Tabaro G.^, Borghese O.^, De Paoli A.*, Frustaci S.°

*°Medical Oncology B Division, ^Clinical Trial Office, *Radiotherapy Division, IRCCS, Aviano*

Aim. Purpose of this study was to assess safety of GEMOX and efficacy of combined CT-RT treatment in patients with locally advanced non-metastatic unresectable pancreatic cancer.

Patients and methods. Between July 2008 and October 2010, 18 patients (pts) with cyto-histologically confirmed pancreatic adenocarcinoma were included. Median age was 57 years (range 33-74), 9 male and 9 female; 15 pts had primary tumour located in the head, 2 in the body and 1 in the papilla of Vater. Patients received 3 cycles of G 1000 mg/m^2 on day 1, 8, 15 and O 100 mg/m^2 on day 1, 15 in a 28 days cycle followed by radiotherapy (RT) 51, 75 Gy in 23 fractions with concurrent G infusion. Tumour lesions were assessed by computed tomography scan (CT scan) after chemotherapy (CT) and after RT treatment. The primary endpoints included objective tumour-response, progression-free survival (PFS) and toxicity. Secondary endpoint was overall survival (OS).

Results. Sixteen of 18 pts are evaluable for toxicity and response; 2 pts are still in therapy. All patients received 3 planned cycles of CT. Average dose intensity was 0.75 (range 0.47-1). Grade 3/4 CT-related toxicities were neutropenia 34%, thrombocytopenia 20%; no toxic death occurred. Grade 1/2 toxicities were anemia 7%, neutropenia 33%, thrombocytopenia 27%, nausea/vomiting 27%, paresthesia 20%, fatigue 13%, diarrhea 20%. CT scan after CT demonstrated 7% of partial remission >30%; 50% of partial remission <30%; 31% of stable disease; 12% of progression disease. Final restaging (after CT-RT) showed 7% of partial remission >30%; 36% of partial remission <30%; 14% of stable disease and 43% of progression disease. One pt received a radical surgery and she is still disease-free. The objective response rate was 7% while clinical benefit was obtained in 57%. Median PFS and median OS survival were 6.48 and 11.3 months, respectively.

Conclusion. These results support the safety of combined CT-RT regimen with a clinical control of disease in this setting of patients.

C28 NON-HEPATIC CANCER (NHC) AND CIRRHOSIS: TO TREAT OR NOT TO TREAT?

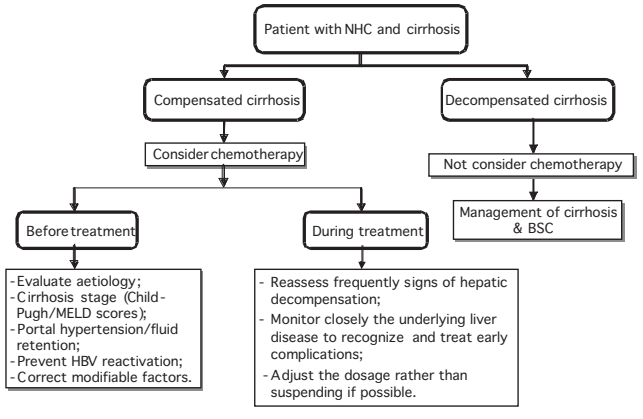
Palmeri L.*, Cabibbo G.^, Craxì A.^, Lo Monte A.*, Buscemi G.*, Vaglica M.*, Di Noto L.*, Bongiovanni A.*, Ancona C.*, Marchese A.*, Palmeri S.*

**Dipartimento di Discipline Chirurgiche ed Oncologiche, ^Dipartimento di Biopatologia e Metodologie Biomediche, Università degli Studi di Palermo*

To date, the appropriate strategy for effective and safe chemotherapy treatment of cancer patients with compensated cirrhosis has not been defined.

Usually clinical trials exclude patients with impaired hepatic function, as a consequence available knowledge about individual chemotherapeutic agents in the setting of cirrhosis is based on small, retrospective studies. Few agents have undergone formal phase1 including patients with liver dysfunction, while empirical guidelines are used in clinical practice. In our opinion, the lack of evidence-based data may lead to deny antitumour treatment to compensated cirrhotic patients. In the absence of any guideline, the physician who decide to treat a NHC in a patient with compensated cirrhosis is burdened both by the narrow therapeutic index, if any, of cytotoxic drugs and the complicated safety issues typical of such patients. We think that this clinical dilemma might be solved overcoming, in principle, the prejudice that a cirrhotic patient cannot be treated if he develops a cancer other than HCC. Clinicians, health authorities and regulatory agencies must start including, or require inclusion of patients with compensated cirrhosis in controlled trials when investigating an anticancer medical treatment.

It is our opinion that: 1) before starting chemotherapy, physicians should: a) evaluate liver disease etiology (viruses, alcohol, others); screen stage (Child-Pugh, MELD scores), portal hypertension, fluid retention (i.e. the prognostic expectation of the liver disease); b) prevent viral reactivation with lamivudine (HBV); c) start correction of modifiable factors (alcohol; other hepato-



toxins; diabetes). 2) during chemotherapy, physicians should: a) frequently evaluate the effectiveness of cancer treatment and carefully monitor the onset of signs of hepatic decompensation; b) adjust the dosage rather than suspend cytotoxic therapy; c) closely assess the underlying liver disease in order to recognize and treat early complications. 3) as concerns liver disease treatment, no changes needed. IFN-based antiviral therapies must be avoided or postponed in this setting.

C29 ADJUVANT CHEMORADIOTHERAPY (CRT) FOLLOWING SURGICAL RESECTION FOR HIGH RISK PANCREATIC ADENOCARCINOMA (PAC) PATIENTS: A RETROSPECTIVE ANALYSIS

Veccia A.[1], Soini B.[1], Caffo O.[1], Frisinghelli M.[1], Pani G.[2], Caldara A.[1], Brugnara S.[1], Dipasquale M.[1], Ferro A.[1], Murgia V.[1], Valduga F.[1], Galligioni E.[1]

[1]Medical Oncology, [2]Radiotherapy, Santa Chiara Hospital, Trento, Italy

Introduction. The role of adjuvant therapy for pancreatic cancer is unclear. Many studies investigated both chemotherapy (CT) and chemoradiotherapy (CRT) as possible options of treatment. However data on CRT are controversial. In this retrospective study we report our experience on high risk patients (pts) with resected pancreatic adenocarcinoma treated with adjuvant 5-fluorouracil (5-FU) or gemcitabine (GEM) based CRT.

Patients and methods. We reviewed a consecutive series of 25 patients who underwent pancreatoduodenectomy or partial pancreatectomy for PAC and were treated with adjuvant 5-FU or GEM based CRT at our institution from January 2000 to May 2011. Seventeen were male and eight female with a median age of 66 years (range 43-80) and a median ECOG PS of 0 (0-2). Thirteen pts were treated with 5-FU based CT (5-FU 250 mg/m^2/die in continuous infusion for 42 consecutive days) and twelve with GEM based CT (GEM 300 mg/m^2 weekly). Radiotherapy was given concurrently to CT for a total dose of 50.4 Gy in 28 fractions. All patients were considered at high risk of relapse: 20 pts (80%) had T3-T4 tumour, 16 pts (64%) had nodal metastases and 14 (56%) had positive or close margins.

Results. CRT treatment was well tolerated, irrespective of chemotherapy with 5-FU or GEM and without G3-G4 toxicities. The median DFS was 10 months (95% CI 6-14), without difference between R0 and R1 margin groups (10 vs 9 months; p = 0.43). The median overall survival was 19 months (95% CI 9-29) and the difference was again not significant between the two groups, although a trend favoured R0 group (30 vs 17 months; p = 0.34).

Conclusions. In spite of the small sample assessed in this survey, our data seems to support the efficacy of adjuvant CRT for high risk PAC. Patients with large tumour burden and/or lymph nodal involvement with or without R1 resection margins could benefit from the combined treatment. Our results are comparable to published data from similar studies.

C30 REDUCED DOSE OF DOCETAXEL MONOTHERAPY AS SALVAGE TREATMENT IN ADVANCED GASTRIC CANCER

Fontana E., Pucci F., Camisa R., Rapacchi E., Leonardi F., Negri F.V., Ardizzoni A.

Medical Oncology Unit, University Hospital of Parma, Parma, Italy

Background. Docetaxel has shown promising activity in advanced gastric cancer (AGC) as salvage chemotherapy. Doses frequently employed in second-line treatments have been 100 mg/m^2 and 75 mg/m^2, with mOS ranging from 6 to 8.3 months. Weekly schedule obtained 3.5 months of mOS.

The purpose of our study is to investigate the efficacy and safety of docetaxel 60 mg/m^2 monotherapy.

Materials and methods. Thirty-one patients with progressing disease, after first-line platinum based chemotherapy, were treated with docetaxel 60 mg/m^2 intravenously with dexamethasone prophylaxis, every three weeks, for a maximum of 8 courses. Bone-marrow, liver and renal functions were assessed after ten days from docetaxel administration. Treatment was stopped in case of disease progression or severe toxicity.

Results. A total of 131 cycles of docetaxel were administered (median 3.7; range 1-8): one patient was not evaluable for response and twenty-two patients (64.5%) progressed. 25.8% obtained stable disease. mTTP was 2.76 months (95% CI, 1.91-3.62) and mOS since the start of docetaxel was 5.26 months (95% CI, 2.14-8.38) with 22.6% of 1-year survival rate. Seven patients (22.6%) experienced G 3-4 neutropenia, but none of them needed hospitalization or G-CSF administration. 15.3% of cycles were administered with 20% of dose-reduction. No chemotherapy related toxic death was observed. Other non-haematological toxicities were relatively mild. An univariate analysis showed that ECOG performance status (2 versus 0 or 1) correlated with TTP (HR: 2.88) and OS (HR: 3.59).

Conclusions. Reduced dose of docetaxel in second-line treatment of AGC patients is feasible and well tolerated. Although no objective responses were seen in our study, median survival is similar to that already observed with other more toxic chemotherapy regimes. Performance status 2 patients have a poor outcome and could be spared second-line chemotherapy.

C31 WEEKLY TCF (W-TCF) AS FIRST-LINE THERAPY IN ADVANCED GASTRIC CANCER: OUR EXPERIENCE

Traficante D., Assalone P., Calista F., Tomei F., Di Lullo L.

ASReM-U.O.C. Oncologia "Giovanni Paolo II", Ospedale "F. Veneziale", Isernia

Background. Gastric cancer is the second most common cause of cancer death worldwide. Approximately two thirds of patients (pts) present with locally advanced or metastatic disease diagnosis. In this setting, chemotherapy vs BSC increases survival and a further benefit has been shown with the latest docetaxel based triplets vs ECF. The treatment related toxicity is a major issue for PS, age, nutritional status, comorbidities and previous surgery. It can improve safety by changing the treatment schedule without compromising the therapeutic outcome. We retrospectively evaluated the toxicity and clinical response in pts with advanced gastric cancer treated with w-TCF.

Methods. From December 2006 to December 2010, 15 chemo naïve pts with advanced gastric cancer received w-TCF (docetaxel 30 mg/m^2 d1, 8, cisplatin 60 mg/m^2 d1, 5-fluorouracil 200 mg/m^2/die continuous infusion, every 21 days). The pts character-

istics are reported in Table 1. Response evaluation was performed every three cycles (cys) with TB CT and EGDS in pts who had not undergone surgery on the primary site. Adequate parenteral nutritional supportive care was administered in two pts.

Results. The results in terms of toxicity and response are reported in Table 2. Thirteen pts received six cys. Two pts have suspended the treatment for peritoneal and liver progression after three and five cys respectively. Dose reduction has not been required, there was not neutropenic fever (FN). G-CSF support was necessary in one patient.

Table 1 - Characteristics of patients

Characteristic	No.
Median age (range)	58 (37-78)
PS (ECOG) 1-2	15
M/F	8/7
Metastatic sites	
Liver	2
Lymph nodes	1
Peritoneum	3
Lung	2
2 or more	7
Prior surgery	
Yes	5
No	10

Table 2 - Results

Results	No.
Safety (G3-G4)	
Anemia	2
Granulocytopenia	1
FN	none
Vomiting	1
Fatigue	2
Diarrhea	1
Stomatitis	1
Response	
Complete	none
Partial	5
Stable	6
Progressive	4

Conclusions. w-TCF has shown a good toxicity profile and, according to the literature, it appears a feasible and effective treatment option in advanced disease.

C32 A MULTIDISCIPLINARY APPROACH FOR NEUROENDOCRINE TUMOURS AT THE ITALIAN ENETS CENTER OF EXCELLENCE OF THE FONDAZIONE IRCCS ISTITUTO TUMORI OF MILAN

Buzzoni R., Coppa J., Pusceddu S., Pelosi G., Milione M., Bombardieri E., Seregni E., Maccauro M., Marchianò A., Spreafico C., Meroni E., Ballardini G., Formisano B., Mazzaferro V.

Italian ENETS Center of Excellence, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Background. Clinical practice has changed over the years with the application of evidence-based methods. Investigations now are measured according to a scale of evidence, guidelines and scores. We believe that for any single patient the best setting of care is a multidisciplinary discussion between specialists in which is given appropriate weight to features specific to individual cases. In Italy about 2,500 new cases of neuroendocrine tumour (NET) are diagnosed yearly. In such heterogeneous neoplasms the treatment options have expanded significantly.

Patients and methods. The therapeutic approach to NETs is the sum of a complex set of management steps in which the know-how of the surgeon, oncologist, radiologist, expert in nuclear medicine, pathologist, endocrinologist and gastroenterologist is intertwined. Starting from September 2010, every two weeks, selected NET cases are discussed in the presence of NET-specialist physicians, in a multidisciplinary meeting named "Tumour Board". Responsibility of any component of the tumour board is clearly identified as well as a referring leadership.

Results. Up to now we evaluated about ninety patients with gastroenteropancreatic NET. All patients are followed in our Institution, where are admitted about 180 new cases yearly. In particular, the main objective of our tumour board is to achieve an interdisciplinary decision on therapy measures according to applicable guidelines while taking the individual needs of the patient into account. A further endpoint is to select, through multifarious discussion, eligible cases for prospective clinical studies and/or experimental projects focused on translational research. In the December 2010 our tumour board was certified as one of the sixteen European ENETS (European Neuroendocrine Tumour Society) Centers of Excellence.

Conclusion. A multidisciplinary approach can assist in providing a coordination of care that is crucial to achieve improvement outcomes in the management of these complex patients. The present call for a revised attitude towards the need for leadership and acceptance of responsibility might assist in keeping this common multidisciplinary effort for our patients as a worthwhile exercise.

C33 ANTITUMOUR ACTIVITY OF SORAFENIB IN HEPATOCELLULAR CARCINOMA PATIENTS

Dettori M.[1], Frau B.[1], Cossu Rocca P.[2], Pascale R.M.[3], Aloi M.B.[1], Lanzillo A.M.[1], Mascia L.[1], Farris A.[4]

[1]Division of Medical Oncology, Gastrointestinal Cancer Unit, "Businco" Hospital, Cagliari; [2]Department of Pathology, [3]Department of Biomedical Sciences, Division of Experimental Pathology and Oncology, [4]Unit of Medical Oncology, Sassari University

Aim. Sorafenib is an active multikinase and multitargeted anti-angiogenic inhibitor with anti-tumour activity. It was approved in the US and in the EU for the treatment of hepatocellular carcinoma patients. In this study we aimed to evaluate clinical efficacy and tolerability of sorafenib and to correlate neoplastic histologic patterns and molecular expression of VEGF-EGF pathways with response to therapy.

Methods. Untreated patients with histologically proven, advanced hepatocellular carcinoma received oral sorafenib 400 mg

twice daily until progression. Tumour response rate was assessed using Modified Response Evaluation Criteria in Solid Tumours (mRECIST) after 12-16 weeks of treatment and tolerability was evaluated using the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE). Immunohistochemistry was performed with specific antibodies against EGFR, RAS, RAF-1, p70s, HIF-alfa.

Results. From September 2007 to August 2010, 13 patients were included and 3 patients are still ongoing. Median age was 73 years (range 54-82 years), male/female ratio was 12/1; only 15% had an ECOG performance status of 0. Most patients discontinued therapy within 3 months for progressive disease or clinical deterioration but 2 patients were long-survivors with over 30 months of treatment (one patient had a complete response). Sorafenib was fairly tolerated; the most common drug-related adverse events were hand-foot skin reactions, anorexia and asthenia. Dose reduction occurred in 6 patients; two patients were withdrawn from the study due to side effects. No significant correlation between histologic features and clinical outcomes were found.

Conclusion. Results of this trial seem to confirm the efficacy of sorafenib as anti-tumour agent and support a moderate profile of tolerability. The study was limited by its small sample size and short duration, further studies are needed in order to better identify the predictors of treatment response in hepatocellular carcinoma patients.

C34 TRANSARTERIAL CHEMOEMBOLIZATION IN THE PALLIATIVE TREATMENT OF UNRESECTABLE INTRAHEPATIC CHOLANGIOCARCINOMA: A CASE REPORT

Secondulfo M.*, Sorrentino P.*, De Cristofano R.*, Lombardi G., Scibelli A., Lombardi C., D'Angelo S.*

**Liver Unit, Clinical and Experimental Hepatology, Department of Internal Medicine, Radiology and Research Institute of Radiology, S.G. Moscati Hospital, Avellino*

Aim. We describe a case of transarterial chemoembolization (TACE) for unresectable intrahepatic cholangiocarcinoma (ICC).

Materials and methods. A.V., male, 80 years old with a history of HCV chronic hepatitis, hypertension, diabetes type 2, during a follow-up received diagnosis of unresectable ICC on haepatic s5. The diagnosis was obtained with liver biopsy.

ICC was at CEUS and TC significantly hypervascular tumour. ICC size was 3 x 3 cm. In March, A.V. underwent TACE. Patient provided informed consent for TACE. TACE was performed using farmarubicina, lipiodol and polyvinyl alcohol particles. Tumour response was evaluated on the basis of findings on computed tomographic (CT) scans and CEUS using Response Evaluation Criteria in Solid Tumours (RECIST) obtained after 30 days after TACE.

Results. The patient session was one. After TACE patient had not fever, nausea, vomiting and abdominal pain. There were not significant haematological toxicities. CEUS and TC after 30 days of TACE showed a successful tumour necrosis (100%).

Conclusions. TACE is safe and may be effective for the treatment of patients with non resectable cholangiocarcinoma, as reported in the literature. Tumour vascularity is highly associated with tumour response.

C35 THE GOAL OF TREATMENT OF HEPATOCELLULAR CARCINOMA WITH SORAFENIB: THE MANAGEMENT OF SIDE EFFECTS IN THE CLINICAL PRACTICE

D'Angelo S., Secondulfo M., Sorrentino P., De Cristofano R.*

*Liver Unit, Clinical and Experimental Hepatology, *Department of Internal Medicine, S.G. Moscati Hospital, Avellino*

Aim. Sorafenib is used for the treatment in advanced hepatocellular carcinoma (HCC), but adverse effects (AE) often cause the interruption of the therapy. We stress how is important the management of AEs to evaluate the effectiveness of sorafenib.

Patients and methods. This was an observational study of outcomes in the "Pioneer" pts (group A) or "Monitored" pts (group B). From October 2008 to February 2011, 51 patients affected by HCC (male 46, female 5, with a median age of 69 years, with a history of HCV chronic 41, HBV chronic 7, ASH 4) were treated with sorafenib 800 mg/day until progression or unacceptable toxicities. Response was analysed according to the modified RECIST criteria and AEs were recorded according to the common toxicity criteria (scored 0-4).

Results. Patients treated had 7 BCLC stage B, 41 stage C, 50 Child Pugh A, 1 Child Pugh B, 50 PSO 0-1, 1 PSO 2-3. In group A (6 pts), which since the first day received 800 mg/day of sorafenib, 5 (84%) patients have AES (pulmonary embolism, acute pancreatitis, atrial fibrillation with SCA, severe hypertension with encephalopathy, abdominal pain) and the therapy was interrupted. In group B (45 pts) 1 patient was lost at follow-up, 7 patients interrupted the therapy for hepatic decompensation, while 37 patients (82%) continued therapy with a stop of HCC progression. Group B pts received 800 mg/day of sorafenib after a median of 21 days. No patients stopped therapy for cardiac, gastrointestinal, haematological, neurological or dermatological, endocrinological AEs. All pts controlled their blood pressure, assumed regular cardiac therapy and they were screened for cardiovascular diseases. No patient with CAD or pulmonary hypertension received sorafenib. Gastrointestinal AES were treated with Fenatinil 25, Racecadotril 100 mg, levosulpiride 25 mg. Drugs given for leukopenia were stopped, before the sorafenib therapy.

Conclusions. In our experience in HCC pts the effectiveness of sorafenib is correctly evaluable if there is a management of pts and sorafenib's AES.

C36 SMALL CELL NEUROENDOCRINE CARCINOMA OF THE ESOPHAGUS ASSOCIATED WITH A SQUAMOUS CELL CARCINOMA. CASE REPORT AND REVIEW OF THE PUBLISHED DATA

Bertoldo E., Biaggi G., Giaretto L., Gattoni E., Muzio A., Oletti M.V., Botta M.

SOC Oncologia, Ospedale Santo Spirito, Casale (AL)

We reported a case of an invasive small cell neuroendocrine carcinoma (SCNC) associated with squamous cell carcinoma *in situ* (SqCCis), without signs of transition. In June 2010 a 77-years-old woman presented disphagia, disphonia and weight loss during the previously 3 months. On examination she showed performance status ECOG 1 and upper abdominal pain.

Esophagoscopy revealed (30 cm from the incisor) a polypoid ulcerated mass 2.5 cm long; biopsies showed pure SCNC (Ki67 = 90%) and in surrounding normal squamous epithelium SqCCis. Immunohistochemical staining confirmed the two different istotypes in different specimens. Chromogranin A circulating was high (209 ng/mL). 18F-FDG positron emission tomography was negative, but 111 In-Pentetreotide scan identified high expression somatostatin 2 and 5 receptors in mesogastric abdomen. Staging computed tomography (TC) was negative. The patient referred to a surgeon for specialist consult: the diagnosis was confirmed after endoscopic ultrasound that did not show regional lymph nodes and confirmed histological features, but the procedure broken the esophagus inducing bleeding. The patient returned in October 2010 because of abdominal pain and poor performance status (ECOG 2). TC abdominal scan revealed liver, iliac and lymph nodes metastases. Under stage IV (TNM) diagnosis of SCNC of the esophagus, chemotherapy with carboplatin (AUC4) on day 1 and etoposide 100 mg/m^2 days 1-2-3 every 21 days was begun; it was complicated by leucopenia G3. After 3 courses progression was found. The patient was treated with a somatostatin analog but she died 2 months later.

From 1952, more than 400 SCNC of the esophagus, characterized by early dissemination and poor prognosis, were reported. Ten of these were associated to SqCC *in situ* and/or invasive, as our report. Distinction between 2 separated identities or a multidirectional differentiation of the same cancer may be difficult. Up to 35% of SCNC of esophagus show mixed features: the hypothesis that SCNC and SqCCis elements arise a late-stage phenomenon in the genetic progression of carcinomas is suggestive.

Session D • Thoracic and lung cancers, head and neck tumours

D1* KRAS MUTATIONAL STATUS STRONGLY IMPACTS PROGRESSION-FREE SURVIVAL OF PATIENTS TREATED WITH PLATINUM BASED CHEMOTHERAPY IN NSCLC. FINAL RESULTS OF A MULTICENTER PROSPECTIVE STUDY

Rulli E.[1], Veronese S.[2], Marsoni S.[3], Bettini A.[4], Farina G.[5], Longo F.[6], Moscetti L.[7], Pavese I.[8], Alabiso O.[9], Bertolini A.[10], Tomirotti M.[11], Farris A.[12], Ferrari V.[13], Martelli O.[14], Lauricella C.[2], Ganzinelli M.[1], Broggini M.[1], Marabese M.[1], Floriani I.[1], Scanni A.[5], Garassino M.C.[5] on behalf of the TAILOR investigators

[1]Oncology Department, "Mario Negri" Institute, Milan, Italy; [2]Pathology Department, Ca' Granda Niguarda Hospital, Milan, Italy; [3]SENDO Foundation, Milan, Italy; [4]Medical Oncology Department, Riuniti Hospital, Bergamo, Italy; [5]Oncology Department, Fatebenefratelli and Ophtalmic Hospital, Milan, Italy; [6]Oncology Division A, Policlinico Umberto I Hospital, Roma, Italy; [7]Oncology Division, Belcolle Hospital, Viterbo, Italy; [8]Oncology Division, San Pietro Fatebenefratelli Hospital, Roma, Italy; [9]Oncology Department, Maggiore della Carità Hospital; Novara, Italy; [10]Medical Oncology Division, Civile Hospital, Sondrio, Italy; [11]Medical Oncology Division, Maggiore Policlinico, Mangiagalli e Regina Elena Hospital, Milan, Italy; [12]Medical Oncology Division, University of Sassari, Sassari, Italy; [13]Medical Oncology Division, Spedali Civili Hospital, Brescia, Italy; [14]Oncology Department, San Giovanni Hospital, Rome, Italy

Background. KRAS mutations in NSCLC are supposed to indicate a poor prognosis and response to anticancer treatment. However, such evidence is only drawn from retrospective series giving controversial results. Moreover, it is possible that the various KRAS mutations differently affect prognosis, carcinogenesis and drug response as demonstrated in preclinical setting.

Aim of this study is to prospectively assess the prognostic value of KRAS mutations in NSCLC patients treated with a first-line platinum containing regimen. This is a properly planned ancillary study within the TAILOR trial (NCT00637910) which is focused mainly on the second-line.

Methods. Tissue and blood samples were collected at diagnosis in the whole cohort of registered patients. KRAS status was centrally determined with standard direct sequencing and KRAS genotype was assessed by real time PCR. The primary hypothesis is a difference in PFS according to KRAS mutational status; the impact of the three more frequent KRAS substitutions (G12C, G12V, G12D) was also explored. The analysis was planned at occurrence of 200 events (HR ≥1.49, power 80%, 2-tailed alpha 10%), in a Cox model adjusting for performance status and radical surgery.

Results. Out of 565 patients registered, 341 (60.5%) were evaluable for KRAS and 85 (25%) were mutated. At a median follow-up of 17 months KRAS mutated patients showed a statistically significant worse PFS (HR 1.42, 95% CI 1.06-1.94; p = 0.02). No differences among doublets were observed in KRAS mutated patients. The most frequent KRAS mutations were: G12C (36.4%), G12V (21.1%), G12D (16.4%), others (25.9%). Prognostic differences among variants are observed. Final genotype analyses are ongoing.

Conclusions. This is the first prospective, pre-planned and adequately sized evaluation of KRAS in NSCLC. Patients mutated for KRAS seem to have a higher risk of progressing. These results suggest that KRAS mutation epidemiology in this setting highly differs from that of colon cancer. Clinical data suggest that tailored strategies for these patients are warranted and our preclinical studies will help in clarifying the molecular mechanisms.

D2* THE RELEVANCE OF DISEASE STABILIZATION (SD) AS A SURROGATE ENDPOINT IN ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS TREATED WITH ERLOTINIB (E) IN SECOND/ THIRD-LINE

Grossi F.[1], Genova C.[1], Barletta G.[1], Rijavec E.[1], Dal Bello G.[1], Pronzato P.[2], Venturino P.[3], Pappagallo G.[4]

[1]S.S. Tumori Polmonari, Istituto Nazionale per la Ricerca sul Cancro, Genova; [2]S.C. Oncologia Medica A, Istituto Nazionale per la Ricerca sul Cancro, Genova; [3]Roche, Italia; [4]Ufficio di Epidemiologia Clinica, Dipartimento di Scienze Mediche, Azienda ULSS 13, Mirano (VE)

Background. SD has often been viewed as a result of uncertain clinical value. With the advent of E in advanced NSCLC, increasing numbers of patients (pts) achieve SD as a best response. In clinical practice is a common observation a high proportion of SD pts receiving E with durable SD. The aim of this analysis was to compare the PFS and OS in pts with advanced NSCLC who achieved confirmed SD or partial response (PR) after second/third-line treatment with E.

Methods. Data from 684 Italian pts, entered into the TRUST trial (Tiseo M et al., Lung Cancer 2008), were analyzed. E was given orally at 150 mg per day and was continued until disease progression, development of unacceptable toxicity or patient's refusal. We define confirmed SD (cSD) if the patients' PFS was >5 months (response to E were per-protocol evaluated every two months).

Results. Pts characteristics: median age 67 years (31-89); females/males = 219/465 (32%/68%); never/former smokers = 191/493 (28%/72%); squamous/adeno/BAC/large cell/NOS = 163/361/26/21/113 (24%/53%/4%/3%/16%); PS 0-1/2-3 = 557/127 (81%/19%). In 83 pts (12%) E was given as first-line therapy in pts unable to receive chemotherapy; 305 pts (45%) had received 1 prior line and 296 (43%) 2 prior lines of chemotherapy. Four hundred and eighty-nine pts were evaluable for response: RR was 11% (5 pts with CR and 47 with PR) and 261 pts (53%) obtained a SD with 161 pts (33%) with cSD. The median PFS estimates (with 95% CI) were 10.7 months (5.3-16.1) for PR pts and 9.9 months (8.1-11.6) for cSD pts (2P-Logrank 0.86). The median OS estimates (with 95% CI) were 24.0 months (12.9-35.1) for PR pts and 18.1 months (14.5-21.6) for cSD pts (2P Logrank 0.30).

Conclusions. Our findings demonstrate for the first time the relevance of achieving disease stabilization with E treatment. Patients obtaining cSD had durable PFS and OS comparable with PFS and OS of those having PR.

D3* GENE EXPRESSION PROFILING OF LUNG ADENOCARCINOMA STAGE I PATIENTS: RISK FOR RELAPSE DISEASE

Siggillino A.[1], Ludovini V.[1], Bianconi F.[2], Pistola L.[1], Piobbico D.[3], Della Fazia A.[3], Tofanetti F.R.[1], Flacco A.[1], Baldelli E.[1], Ragusa M.[4], Bellezza G.[5], Servillo G.[3], Crinò L.[1]

[1]Medical Oncology, S. Maria della Misericordia Hospital, Perugia; [2]Department of Electronic and Information Engineering, Perugia University, Perugia; [3]Department of Clinical and Experimental Medicine University of Perugia; [4]Department of Thoracic Surgery, University of Perugia; [5]Institute of Pathological Anatomy and Histology, Perugia University, Perugia, Italy

Background. Lung cancer is the leading cause of cancer-related death in the world wide. No reliable clinical or molecular predictors are currently available for identifying those at high risk for developing recurrent disease. The aim of the study was to identify novel genes involved in the risk of early relapse (ER) compared to no relapse (NR) disease from lung adenocarcinoma stage I patients.

Material and methods. From tissue banking of 110 consecutive resected NSCLC patients at Santa Maria della Misericordia Hospital in Perugia, we only selected frozen specimens of lung adenocarcinoma tissue from stage I patients.

We compared gene expression profiling from normal lung (NL) and cancer specimens from NR and ER, using Affimetrix human microarray HG-U133Plus 2.0. We applied principal component analysis (PCA) combined with clustering methods to select the significant genes. We validated selected genes up- and down-regulated by quantitative-PCR (Q-PCR).

Results. Microarray analysis had shown a panel of 223 differentially expressed genes (84 up- and 139 down-regulated). Based on the fold change ratio of ER vs NR, we selected 51 genes (20 up- and 31 down-regulated). The results of genes expression in Q-PCR were superimposable compared to those of microarray analysis ($p = 0.0038$). The 51 selected genes were evaluated one by one in the 18 patient samples (13 NR and 5 ER) by Q-PCR: 74.2% and 80% of the up- and down-regulated genes, respectively, were predictive for clustering patients in ER and NR.

Conclusion. Our results indicate that it is possible to define, through gene expression, a characteristic gene profiling of early relapse tumour patients with an increased risk of relapse disease. Among the identified genes (up-regulated: INSL4, CLCA2, FABP3, GLYATL2, IL1RL1 and down-regulated: XIST, OLFM4, GSTA1, SCGB1A1, IGHD) several are already known in tumour pathways and others could be new potential targets. To further validate our results we will use an independent cohort of patients with lung adenocarcinoma stage I and the analyses are ongoing.

D4* PHASE II TRIAL OF NEOADJUVANT PEMETREXED PLUS CISPLATIN FOLLOWED BY SURGERY AND RADIATION IN THE TREATMENT OF MALIGNANT PLEURAL MESOTHELIOMA (MPM)

Rea F.[1], Favaretto A.[2], Marulli G.[1], Spaggiari L.[3], De Pas T.M.[4], Ceribelli A.[5], Paccagnella A.[6], Crivellari G.[6], Russo F.[7], Ceccarelli M.[7], Facciolo F.[8]

[1]Azienda Ospedaliera di Padova, Div. Chirurgia Toracica, Padova, Italia; [2]Istituto Oncologico Veneto, Div. Oncologia Medica, Padova, Italia; [3]Istituto Europeo di Oncologia, Div. Chirurgia Toracica, Milano, Italia; [4]Istituto Europeo di Oncologia, Div. Oncologia Medica, Milano, Italia; [5]Istituto Nazionale Tumori "Regina Elena", Div. Oncologia Medica, Roma, Italia; [6]Ospedale dell'Angelo, Div. Oncologia Medica, Mestre (VE), Italia; [7]Eli Lilly Italia, Sesto Fiorentino (FI), Italia; [8]Istituto Nazionale Tumori "Regina Elena", Div. Chirurgia Toracica, Roma, Italia

Background. Combined modality approaches to therapy, including surgery and radiation, have proved feasible and are becoming one of the standards of care in MPM. This study aimed to assess the efficacy of the combination of neoadjuvant pemetrexed + cisplatin, extrapleural pneumonectomy (EPP) and hemithoracic radiation (HTR) in MPM.

Methods. This was a multicenter, phase II, open-label study with event-free survival (EFS) (defined as time from enrollment to first observation of disease progression, death due to any cause or early treatment discontinuation) as the primary endpoint.

Between 2005 and 2008, 56 patients with MPM (T1-3, N0-2) were screened, of whom 54 were enrolled (87% male; median age 63 [range 39-75] years; ECOG PS 0-1; adequate organ function).

Pre-operative pemetrexed 500 mg/m^2 + cisplatin 75 mg/m^2 IV was given every 21 days x 3 cycles, plus folic acid, vitamin B12 and dexamethasone, followed by EPP and HTR (total dose 54 Gy).

After 2 deaths due to cardiopulmonary failure, occurred after HTR therapy (21/54 [38.8%] patients were already enrolled in the study at this time), the protocol was amended reducing HTR dose to 50.4 Gy.

Results. Fifty-two/54 (96.3%) patients completed chemotherapy, 45/54 (83.3%) underwent surgery, 22/54 (40.7%) completed the whole treatment including 90-day follow-up. The median EFS was 6.9 months (95% CI 5.0-10.5) and the median progression-free survival was 8.6 months (95% CI 6.3-14.4). A total of 18/54 (33.3%) and 13/54 (24.1%) patients were still event-free after 1 and 2 years respectively. Sixteen/54 (29.6%) patients showed partial response to chemotherapy, 31/54 (57.4%) showed stable disease, 4/54 (7.4%) showed progression, responses in 3/54 (5.6%) patients were unknown (overall response before surgery).

During the whole study 36/54 (66.7%) patients experienced ≥1 grade 3-4 toxicity (the most frequent were hematological and gastrointestinal) but no statistically significant differences were observed before and after amendment.

Conclusions. These results are aligned with the available scientific literature related to the trimodality approach on MPM, showing that the adopted multidisciplinary treatment is effective with a manageable toxicity profile.

D5* CONCOMITANT CHEMORADIATION IN LOCALLY ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMA: A LITERATURE BASED META-ANALYSIS ON THE EFFECT OF CISPLATIN TOTAL DOSE AND PLATINUM COMPOUNDS

Ghi M.G.[1], Paccagnella A.[1], Floriani I.C.[2], Garavaglia D.[2], Chiappa F.[2], Mastromauro C.[3]

[1]Medical Oncology Department, Venezia, Italy; [2]Laboratory of Clinical Trials, Oncology Department, Mario Negri Institute, Milano, Italy

Purpose. Concomitant platinum-based chemoradiation (RT + CHT) is the standard treatment for locally advanced head and neck cancer. No consensus regarding the optimal concomitant platinum-based regimen exists.

Methods. Randomized trials comparing radiation alone (RT) vs concomitant platinum-based RT+CHT were identified by Medline search covering January 1980 to September 2010. The main endpoints were to compare the effect on overall survival (OS) of different cisplatin (DDP) total dose and platinum compounds (cisplatin vs carboplatin), and to analyze the interaction of platinum compounds and DDP dose on acute grade 3-4 mucositis.

Results. Fifteen randomized trials (2502 patients) fulfilled the eligibility criteria. No difference in OS was observed between DDP = 300 mg/m^2 (HR 0.59, 95% CI 0.46-0.74) and DDP <300 mg/m^2 plus 5-fluorouracil (5FU) (HR 0.59, 95% CI 0.45-0.77) when compared to RT alone. The HR of death was 0.68 (95% CI 0.54-0.86) for DDP at intermediate dose (>150 and <300 mg/m^2) without 5FU, 1.04 (95% CI 0.85-1.27) for DDP <150mg/m^2 without 5FU and 0.69 (95% CI 0.59-0.79) for carboplatin-based chemotherapy. The indirect comparison showed the absence of a difference in benefit between DDP at any dose and Cb (HR 0.90, 95% CI 0.72-1.11). The grade 3-4 mucositis incidence was 57% for concomitant DDP = 300 mg/m^2, 46.1% for DDP <300 mg/m^2 plus 5FU (p = 0.023), and 45.9% for concomitant carboplatin studies (p = 0.096).

Conclusions. Our metanalysis seems to suggest that there is a dose/efficacy relation for concomitant cisplatin total dose. Concomitant DDP <300 mg/m^2 in combination with 5FU gives the same survival benefit of concomitant DDP = 300 mg/m^2, with a significant lower incidence of grade 3-4 mucositis. Chemoradiation with carboplatin and cisplatin, independently from doses and schedules, seems to give the same survival advantage over RT alone with a similar G3-4 mucositis incidence.

D6* PEMETREXED VERSUS PEMETREXED PLUS CARBOPLATIN IN PRETREATED PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER: A POOLED ANALYSIS OF TWO RANDOMIZED TRIALS

Tiseo M.[1], Ardizzoni A.[1], Boni L.[2], Vincent A.[3], Buti S.[4], Camerini A.[5], Labianca R.[6], Genestreti G.[7], Zanelli F.[8], Ciuffreda L.[9], Di Costanzo F.[10], de Marinis F.[11], Crinò L.[12], Santo A.[13], Pazzola A.[14], Barbieri F.[15], Zilembo N.[16], Colantonio I.[17], Tibaldi C.[18], Smit E.[19] on behalf of GOIRC and NVALT groups

[1]Azienda Ospedaliero-Universitaria di Parma; [2]Istituto Toscano Tumori; [3]Netherlands Cancer Institute; [4]Istituti Ospitalieri, Cremona; [5]Lido di Camaiore, Lucca; [6]Ospedali Riuniti di Bergamo, [7]IRST, Meldola; [8]Arcispedale S. Maria Nuova, Reggio Emilia; [9]Ospedale S. Giovanni Battista-Molinette, Torino; [10]Azienda Ospedaliero-Universitaria Careggi, Firenze; [11]Ospedale San Camillo-Forlanini, Roma; [12]Azienda Ospedaliera di Perugia; [13]Azienda Ospedaliero-Universitaria di Verona; [14]ASL1, Sassari; [15]Policlinico di Modena; [16]Istituto Nazionale Tumori, Milano; [17]Azienda Ospedaliera Santa Croce e Carle, Cuneo; [18]Ospedale di Livorno; [19]VU University Medical Center, Amsterdam

Background. To evaluate the benefit of adding carboplatin to single-agent pemetrexed chemotherapy in 2nd-line treatment of advanced NSCLC, by pooling the results of two identical phase II randomized trials (GOIRC 02.2006 and NVALT-7 trials) carried out in Italy and The Netherlands, respectively.

Methods. Main eligibility criteria in both trials were: diagnosis of advanced NSCLC, disease progression after 1st-platinum-based chemotherapy, normal organ function and ECOG performance status 0-2. Patients were randomized to receive pemetrexed 500 mg/m^2 alone or combined with carboplatin (AUC5). Cycles were repeated every 3 weeks for a maximum of 4 courses. Both studies were designed to detect a 33% decrease in the hazard of disease progression in the combination arm. The pooled analysis was pre-planned and designed to assess the impact of adding carboplatin to pemetrexed in terms of overall survival (OS) in the overall population and in certain subgroups.

Results. A total of 479 patients were randomized in the two trials. Main patients characteristics were: male gender 68%, median age 62 (range 36-84), PS 0/1 45/49%, squamous cell histology 19%, stage IV 79%, interval from last 1st-line chemotherapy course and randomization ≥3 months in 71% of patients (42% ≥6 months), prior response to 1st-line chemotherapy 50%. Despite identical eligibility criteria in the two studies, there was heterogeneity for some clinical characteristics (more squamous tumours, more advanced PS, longer treatment-free interval in the Dutch study). In the overall population, survival was not improved by the addition of carboplatin to pemetrexed; the HR for death was 0.88 (95% CI 0.71-1.07; p = 0.202; p for heterogeneity = 0.693). Objective response rate was increased in the carboplatin-containing arm with an OR of 1.78 (95% CI 1.01-3.12; p = 0.046; p for heterogeneity = 0.060). A non-statistically significant increase in PFS favouring combined chemotherapy was observed with a HR of 0.85 (95% CI 0.71-1.02; p = 0.082; p for heterogeneity = 0.019). In the subgroup analyses, there was a statistically significant interaction between histological subtype and treatment: in fact, the addition of carboplatin to pemetrexed in patients with squamous tumours led to a statistically significant improvement of PFS from 2 to 3.2 months (adjusted HR: 0.42; 95% CI 0.27-0.65; p of interaction test = 0.001) and of OS from 5.4 to 9 months (adjusted HR: 0.57; 95% CI 0.36-0.90; p of interaction test = 0.05).

Conclusions. Single agent pemetrexed remains the standard of care 2nd-line chemotherapy in patients with relapsed non-squamous lung tumours. Although pemetrexed has presently no indication in the treatment of squamous subtype NSCLC, the results of this pooled analysis can support further investigation of the carboplatin-pemetrexed regimen in the 2nd-line treatment of this histological subtype.

D7 *MYC* AND HUMAN TELOMERASE GENE (*TERC*) AMPLIFICATION IN EARLY STAGE NON-SMALL CELL LUNG CANCER (NSCLC)

Ludovini V.[1], Flacco A.[1], Bianconi F.[2], Tofanetti F.R.[1], Ragusa M.[3], Vannucci J.[3], Bellezza G.[4], Mameli M.G.[4], Metro G.[1], Pistola L.[1], Siggillino A.[1], Baldelli E.[1], Sidoni A.[4], Puma F.[3], Varella-Garcia M.[5], Crinò L.[1]

[1]Medical Oncology Department, S. Maria della Misericordia Hospital, Perugia, Italy; [2]Department of Electronic and Information Engineering, [3]Department of Thoracic Surgery, [4]Institute of Pathological Anatomy and Histology, University of Perugia, Perugia, Italy; [5]Department of Medicine/Medical Oncology, University of Colorado Cancer Center, Aurora, CO

Background. Long-term survival of early NSCLC is disappointing and targets for a new generation of therapeutic agents are necessary. Abnormalities in *MYC* are well known in lung cancer. *TERC* maps in chromosomal region with frequent copy number gain (CNG) in NSCLC. This study investigates the incidence of *MYC* and *TERC* CNG and evaluates their correlation with clinicopathological parameters and outcome in early stage NSCLC.

Methods. 113 NSCLC patients subjected to curative pulmonary resection were tested for *TERC* and *MYC* CNG by fluorescence *in situ* hybridization (FISH) using commercial probes. Median age was 66 years (range 40-84); most patients were male (84%), former/current smokers (92%), had poorly differentiated histology (42%) and stage I disease (62%). The histological types included 51% squamous cell carcinoma (SCC), 30% adenocarcinoma, 8% BAC, and 11% of other subtypes. CNG was determined when ≥4 gene copies were displayed in ≥40% of tumour cells.

Results. Forty-one (36%) patients showed CNG for *MYC* and 41 (36%) for *TERC*. *MYC* and *TERC* gene amplification (GA) were found in 9 (8%) and 15 (13%) cases, respectively. *MYC* and *TERC* contemporary CNG was observed in 12 cases (11%): 2 (17%) cases with GA vs 10 (83%) high polysomy. *TERC* CNG was associated with SCC histology (80% vs 20% in non-SCC; $p = 0.001$). In univariate analyses, both *MYC* CNG and GA were associated with shorter disease-free survival (DFS, $p = 0.032$ and $p = 0.022$, respectively) and overall survival (OS; $p < 0.032$ and $p < 0.000$, respectively) while *TERC* CNG or GA showed no association. In multivariate analysis including stage and age, *MYC* CNG and GA remained significantly associated with worse DFS ($p = 0.022$; $p = 0.011$ respectively) and OS ($p = 0.026$; $p < 0.000$, respectively).

Conclusions. Our results indicate that *MYC* and *TERC* are frequently amplified in NSCLC. CNG for *MYC* is a strong predictor of worse survival. *TERC* CNG shows phenotypic properties strongly associated with SCC and is not a prognostic factor.

We thank the Italian Association for Cancer Research AIRC (AF Fellowship).

D8 PHASE II STUDY OF AFATINIB (BIBW 2992), AN IRREVERSIBLE erbB FAMILY BLOCKER, IN ADVANCED EGFR FISH POSITIVE NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS

Cappuzzo F.[1], Finocchiaro G.[2], Rijavec E.[3], Bidoli P.[4], Favaretto A.[5], Clementi L.[6], Massey D.[7], Lorence R.[8], Santoro A.[2]

[1]Livorno Hospital, Livorno, Italy; [2]Istituto Clinico Humanitas, Rozzano, Italy; [3]National Institute for Cancer Research, Genova, Italy; [4]S. Gerardo Hospital, Monza, Italy; [5]Istituto Oncologico Veneto-IRCCS, Padova, Italy; [6]Boehringer Ingelheim Italia S.p.A., Milan, Italy; [7]Boehringer Ingelheim Limited, Bracknell, Berks/GB; [8]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT/US

Background. Afatinib (A), an irreversible erbB family blocker, has previously shown to have a high response rate in NSCLC patients (pts) with EGFR mutations. Whether this activity extends to those pts with EGFR FISH positive tumours is not known. We conducted a multicenter phase II study to evaluate efficacy of A in advanced NSCLC pts with increased EGFR gene copy number.

Methods. NSCLC pts who received 0 or 1 cytotoxic treatment for advanced disease were screened for EGFR gene amplification and/or high polysomy. Study entry was restricted to pts with stage IIIB/IV, PS 0-2, and no prior TKI therapy. Enrolled pts were treated with A (50 mg, daily oral dosing). Patients with available tumour tissue were tested for common EGFR mutations in exons 19 and 21 by PCR single-strand conformation polymorphism analysis and direct sequencing. The primary endpoint was ORR per RECIST.

Results. 69 EGFR FISH+ pts have so far received A: 41 as first line, 28 second line. 52% were men, median age was 67 yrs, and only 30% were never-smokers. Among 54 evaluable pts, there were 11 responses to A (1 CR and 10 PRs; confirmed thus far in 7) for an ORR of 20%. Among responders, 5 of 8 pts have tested negative for EGFR mutations. Of the eight pts with stable disease (SD) for at least 16 weeks, 6 of 6 have tested negative for EGFR mutations including one pt continuing treatment at 96+ weeks. Overall, 36% of pts had disease control lasting at least 16 weeks. The safety profile of A was similar to that in previous trials: diarrhea and rash/acne were the two most common adverse events and were effectively managed by supportive care and/or dose reduction.

Conclusions. In this phase II trial in EGFR FISH+ advanced NSCLC pts, afatinib showed encouraging activity and acceptable toxicity. EGFR mutation results have so far been negative for most responders and all pts with SD of at least 16 weeks duration. Further investigations of afatinib in NSCLC pts with EGFR FISH+ tumours are warranted especially as efficacy in non-mutated pts has been observed in this trial.

D9 QUALITY OF LIFE RESULTS OF THE TORCH RANDOMIZED PHASE III TRIAL: FIRST-LINE ERLOTINIB FOLLOWED BY SECOND-LINE CISPLATIN + GEMCITABINE VERSUS REVERSE SEQUENCE IN ADVANCED NON-SMALL CELL LUNG CANCER

Di Maio M.[1], Leighl N.[2], Signoriello S.[3], Rossi A.[4], Gebbia V.[5], Morgillo F.[3], Wierzbicki R.[6], Favaretto A.[7], Alam Y.[8], Cinieri S.[9], Siena S.[10], Marciano R.[11], Cartenì G.[12], Spatafora M.[13], Ravaioli A.[14], Maione P.[4], Butts C.[15], Ciardiello F.[3], Feld R.[2], Gallo C.[3], Perrone F.[1], Gridelli C.[4] on behalf of the TORCH investigators

[1]National Cancer Institute, Napoli, Italy; [2]Princess Margaret Hospital, Toronto, Canada; [3]Second University, Napoli, Italy; [4]S.G. Moscati Hospital, Avellino, Italy; [5]La Maddalena Clinic, Palermo, Italy; [6]Durham Regional Cancer Centre, Oshawa, Canada; [7]Istituto Oncologico Veneto, Padova, Italy; [8]Windsor Regional Cancer Centre, Windsor, Canada; [9]A. Perrino Hospital, Brindisi, Italy; [10]Niguarda Ca'Granda Hospital, Milano, Italy; [11]University Federico II, Napoli, Italy; [12]A. Cardarelli Hospital, Napoli, Italy; [13]Ospedali Riuniti Villa Sofia Cervello, Palermo, Italy; [14]Ospedale degli Infermi, Rimini, Italy; [15]Cross Cancer Institute, Edmonton, Canada

Background. The TORCH randomized phase III trial tested whether, in patients with advanced NSCLC, overall survival (OS) with first-line erlotinib followed by second-line cisplatin + gemcitabine was not inferior than with the standard, reverse sequence. Primary analysis showed significantly worse OS in experimental arm (Gridelli, AIOM 2010, abstr 3). Quality of life (QoL) was among secondary endpoints.

Methods. QoL analysis was limited to first-line treatment. EORTC QLQ-C30 and QLQ-LC13 had to be compiled at baseline and every 3 weeks. For each domain or symptom: 1) differences from baseline were described at 3, 6 and 9 weeks; 2) best response from baseline was calculated according to the Osoba method; 3) time-to-deterioration was estimated using the competing risk approach, because of the great survival difference, and treatments compared with the Gray method.

Results. 630 out of 760 randomized patients compiled baseline questionnaire, 315 (83%) in each arm. Baseline characteris-

tics were well balanced between arms. Females were 33.7%; 55.5% had adenocarcinoma; 20.7% were never-smokers. Compliance of QoL questionnaires at 3, 6 and 9 weeks was 78%, 61% and 45% with erlotinib; 79%, 71% and 58% with chemotherapy. Compliance was largely affected by different survival and progression rates between arms; indeed, compliance among patients without disease progression or death was similar between arms. Mean differences from baseline in global QoL score were -1.45, -2.84 and -3.27 with erlotinib, and 0.22, 0.56 and -0.16 with chemotherapy, at 3, 6 and 9 weeks respectively. Improved, worsened and stable patients in global QoL according to Osoba method were 31%, 40% and 29% with erlotinib, 36%, 34% and 30% with chemotherapy ($p = 0.27$). Time-to-deterioration of global QoL was not different between arms ($p = 0.56$). Significant differences in response/deterioration patterns were observed for pain, sleeping disorders, diarrhea, dyspnea (better with chemotherapy); nausea/vomiting, constipation, sore mouth and alopecia (better with erlotinib).

Conclusions. Interpretation of QoL analysis was largely affected by differences in survival and progression between arms. Treatment did not differently affect functional scales and global QoL, some symptoms were controlled better with chemotherapy, side effects were consistent with expected toxicity profile.

Partially supported by Roche.

D10 ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS TREATED WITHIN OR OUTSIDE CONTROLLED CLINICAL TRIALS: TOXICITY PROFILE AND SURVIVAL DATA

Rovere G., Vavalà T., Longo M., Capelletto E., Rapetti S.G., Crida B., Novello S.

University of Turin, AOU San Luigi-Orbassano (TO)

Background. The common perception is that the inclusion of patients with cancer in clinical trials leads to improved outcomes, even if there aren't clear data to make a statement about this issue. We conducted a single institution retrospective analysis evaluating survival data and toxicity profile in NSCLC patients treated with standard therapy or within controlled clinical trials.

Methods. We analysed 300 consecutive patients treated at the Thoracic Oncology Unit of San Luigi Hospital from 2004, January the 1st to 2010, December the 31st, having these characteristics: histo/cytological diagnosis of NSCLC, stage IV, who received at least 3 chemotherapy cycles, with a minimum follow-up of six months. In this population 178 patients (59%) were enrolled in controlled clinical trials (T) while 122 (41%) were treated with standard therapy (S).

Results. The most important differences between the two groups were about median age at the time of starting first-line treatment (61.2 in group T vs 64 years in group S), patients over 70 years (19% vs 27%, respectively) and ECOG/PS distribution (PS = 2: 0 vs 9 patients, PS = 1: 33 vs 53 patients, PS = 0: 145 vs 60 patients in T and S group, respectively). Looking at the different lines of therapy in T population: in patients enrolled in first-line clinical trials only, median OS was 9.2 months, 18.1 months in patients enrolled in first- and second-line clinical trials, 15.3 months in patients enrolled only in second-line clinical trials and 26.4 months in patients enrolled in first-, second- and third-line studies. Any relevant differences were seen between group T and S in terms of toxicity.

Conclusions. This single institution retrospective analysis documented a better outcome for patients enrolled in clinical trials compared to those treated with standard therapy (even without a statistical significance) with a higher percentage of patients reaching a second- and third-line therapy. Larger multicenter prospective dedicated studies have to be planned.

Characteristics	Group S	Group T
Patients eligible for second-line treatment	43 (35%)	105 (59%)
Patients eligible for third-line treatment	18 (15%)	45 (25%)
OS (months)	9.5	13.5
PFS (months)	6.3	7.1

D11 NEW COMBINED TREATMENT SCHEMES IN LOCALLY ADVANCED NASOPHARINGEAL CARCINOMA OBSERVED IN A NON-ENDEMIC POPULATION

Raimondo L.[1], Airoldi M.[2], Garzaro M.[1], Pedani F.[2], Riva G.[1], Pecorari G.[1], Giordano C.[1]

[1]1st ENT Division, Physiopathology Department, University of Turin, Turin, Italy; [2]2nd Medical Oncology Division, San Giovanni Battista Hospital, Turin, Italy

Purpose. Aim of this study was the clinical evaluation of two different schemes of neoadjuvant chemotherapy (NACT) followed by concomitant chemoradiotherapy (CHRT) in locoregionally advanced nasopharyngeal carcinoma (A-NPC) in a non-endemic population.

Patients and methods. Seventy patients (51M, 19F, median age: 53.5 yrs, median ECOG PS: 0 (63 pts) and 1 (7 pts); 63 pts type 3 and 7 pts type 2 WHO histology; 36 pts stage III, 28 pts stage IVa and 6 pts IVb AJCC TNM; 47 pts N2/N3 AJCC TNM) were enrolled. Forty pts (A) were treated with 3 cycles of NACT with cysplatin (100 mg/m^2) + epirubicin (90 mg/m^2), followed by cysplatin (100 mg/m^2) and concomitant 70 Gy RT; 30 (B) received 3 cycles of NACT with carboplatin (AUC6) + taxol (175 mg/m^2) followed by carboplatin (AUC1) + taxol (60 mg/m^2) and concomitant 70 Gy RT.

Results. (%A vs %B). After IC: complete responses (CRs 30% vs 33%), partial responses (PRs 60% vs 60%), no change (NC 10% vs 6.6%); after CHRT: CRs (75% vs 87%), PRs (25% vs 13%). After a median follow-up of 54 months (A) and 49 months (B): 3 and 5 years progression-free survival was 75% vs 80% and 65% vs 75% respectively and overall survival was 84% vs 85% and 77% vs 80% respectively; 5 years locoregional control was 70% vs 90% and 5 years distant metastases-free survival was 75% vs 85%; toxicity of IC was: G3-G4 neutropenia 40% vs 83%, G3 thrombocytopenia 12% vs 13%, G3 anaemia 0% vs 10% and G3 mucositis 2.5 vs 6.6%; toxicity of CHRT was: G3-G4 neutropenia 20% vs 63%, G3 thrombocytopenia 10% vs 7.5%, G3 anaemia 2.5% vs 17%, G3-G4 mucositis 32.5% vs 69%, skin toxicity 25% vs 23% and G3 neurotoxicity 5% vs 10%.

Conclusion. Neoadjuvant chemotherapy with such protocol represents a feasible, efficient treatment for patients with A-NPC, ensuring excellent locoregional disease control and overall survival with low incidence of distant metastases.

D12 THE PHARMACOGENETIC POLYMORPHIRMS IN PREDICTING RESPONSE TO CISPLATIN-BASED CHEMOTHERAPY IN LUNG CANCER PATIENTS

Ferrario S.*, Farè E.*, Filipazzi V.*, Cattaneo M.T.*, Isabella L.*, Gambaro A.*, Tosca N.*, Damiani E.*, Maucieri A.*, De Troia B.*, Cattaneo D.°, Clementi E.°, Radice S.°, Piazza E.*

**Oncology, °Pharmacology Department, "Luigi Sacco" Hospital, Milan, Italy*

Background. Among cancer patient population, resistance to therapy is a major cause of treatment failure. A lot of studies examined the role of polymorphisms regarding genes encoding enzymes involved in drugs' metabolism and in repair of DNA adducts, in the outcome of therapy in terms of toxicity[1]. The present study examined the correlation between the outcome in terms of response of patients with lung cancer after chemotherapy with cisplatin or carboplatin and the presence of genetic polymorphisms in these genes.

Methods. We investigated the potential association of GSTP1 313A >G, XRCC1 28152G >A, ERCC1 8092C >A, ERCC1 19007T >C, ABCB1 3435C >T and their haplotypes with chemotherapy response of 62 patients with advanced lung cancer (13% with SCLC, 10% with mesothelioma and 77% NSCLC), treated with a platinum-based regimen. DNA was extracted from peripheral blood and was evaluated by real time PCR and pyrosequencing. The treatment response was assessed with TC scan after at least 3 chemotherapy sessions. The genotypes were retrospectively correlated with good response (PR) or absent response (SD or PD) to the treatment.

Results. We observed 28 PR in 62 treated patients (45%). The *ABCB1 3435 TT* genotype was present in 9/16 responders, the *ABCB1 3435 CT* in 15/24 and *GSTP1 313 GG* was present in 2/3. They were associated with a significantly better response to chemotherapy, compared with the ABCB1 *3435 CC* 3/14 and *GSTP1 313 AA* genotype 10/23 responders ($p < 0.01$). We also observed a better response in ERCC1 19007 TC patients compared with ERCC1 19007 TT and CC but there wasn't significant correlation. Finally we didn't find significant correlation between response and XRCC1 28152G >A and ERCC1 8092C >A polymorphisms.

Conclusions. Our findings suggest that genetic polymorphisms in ABCB1 and GSTP1 may be a predictive marker of platinum-based treatment response in patients with advanced lung cancer.

References

1. Kalikaki A et al: DNA repair gene polymorphisms predict favorable clinical outcome in advanced non-small cell lung cancer. Clin Lung Cancer, 10 (2): 118-123, 2009.

D13 EPIDEMIOLOGY AND CLINICOPATHOLOGIC FEATURES OF ENDOBRONCHIAL METASTASIS FROM EXTRA-PULMONARY TUMOURS: A FORMIDABLE PITFALL WITH PRIMARY LUNG CANCER

Longo L.[1], Lasagni A.[2], Marchioni A.[2], Busca A.[4], Cavazza A.[5], Migaldi M.[3], Corradini P.[2], Carbonelli C.[6], Cadioli A.[3], Artioli F.[1], Rossi G.[3]

[1]Oncology Division, Civic Hospital of Carpi, AUSL Modena; [2]Respiratory Diseases Clinic, [3]Pathologic Anatomy, Azienda Policlinico of Modena; [4]Thoracic Endoscopy Unit, Ospedale Maggiore, Bologna; [5]Pathologic Anatomy, [6]Pneumology, Arcispedale S. Maria Nuova, Reggio Emilia

Introduction. Tumours growing into the bronchus are generally considered as lung primary, while endobronchial metastases from extra-pulmonary malignancies represent rare events, mainly consisting of anecdotal case reports.

Methods. A detailed clinico-pathologic, retrospective analysis of all bronchoscopy examinations from two different Institutions between 1991-2010 was performed. All bronchial biopsies obtained in the suspicion of cancer were retrieved and reviewed by expert pulmonary pathologists. Leukemic and lymphomatous involvement of lungs were excluded from the study. Specific immunostains were performed in selected cases. Clinical data were also reviewed and statistical analysis was evaluated using Pearson's chi-square and Fisher's tests.

Results. Case series consisted of 199 cases, including 108 males (54%) and 91 females (46%) with a median age of 67 years (range 27-89). Metachronous (extra-pulmonary tumours disclosed before bronchial metastases), synchronous and anachronous (extra-pulmonary malignancy presenting as endobronchial tumour) metastases were observed in 178 cases (89.4%), 11 (5.6%) and 10 cases (5%), respectively. Overall, endobronchial metastases account for 4% of all bronchial biopsies performed when suspecting cancer. Breast cancer (58 cases, 29%) was the commonest extra-pulmonary tumours, followed by colon-rectum (25%), kidney (13%), melanoma (6%) and stomach (5.5%). Other extra-pulmonary metastases were from prostate (n = 9), thyroid (n = 7), endometrium and liver (n = 3), ovary, small intestine, skin leiomyosarcoma (n = 2) and one case each of bladder, cervix, oesophagus, vaginal, renal pelvis, mesothelioma, solitary fibrous tumour, liposarcoma, uterine leiomyosarcoma, nasal-type carcinoma, plasmacytoma, meningioma and basal cell carcinoma. Patients were asymptomatic in 26% and latency period in developing endobronchial metastasis was different among histology with a wide range for breast cancer (17-154 months) and shorter for stomach (12-46 months).

Conclusions. Extra-pulmonary tumours presenting with endobronchial metastasis are rare, but they accounts for about 4% of all bronchial biopsies showing malignancy. Unknown extra-pulmonary neoplasms were detected as endobronchial metastases in 5% of these cases. Considering novel effective histology-based therapies in lung cancer, clinicians and pathologists should keep in mind this occurrence, representing a formidable pitfall with therapeutic consequences.

D14 NUMBER OF RESECTED LYMPH NODES IN EARLY STAGE NON-SMALL CELL LUNG CANCER (NSCLC) PREDICTS PATIENTS SURVIVAL

Berardi R.[1], Onofri A.[1], Savini A.[1], Caramanti M.[1], Chiorrini S.[1], Santinelli A.[2], Brunelli A.[3], Zuccatosta L.[4], Pompili C.[3], Mazzanti P.[1], Pierantoni C.[1], Scartozzi M.[1], Sabbatini A.[3], Gasparini S.[4], Cascinu S.[1]

[1]Clinica di Oncologia Medica, [2]Servizio di Anatomia Patologica, Università Politecnica delle Marche, A.O.U. Ospedali Riuniti, Ancona, Italy; [3]Clinica di Chirurgia Toracica, [4]SOD di Pneumologia, A.O.U. Ospedali Riuniti, Ancona, Italy

Background. Despite an appropriate surgical treatment, half of early stage NSCLC patients will die due to lung cancer. The number of resected lymph nodes has proved prognostic in breast and colorectal cancer. Here we evaluate its prognostic impact in the largest monocentric series of resected NSCLC patients.

Methods. Clinical and pathological characteristics and prognostic outcomes of 439 consecutive patients undergoing radical surgical resection for NSCLC at our Institution between 1996 and 2001 were retrospectively evaluated.

Results. The multivariate analysis showed that smoking history, pathological stage of disease, N status, number of resected lymph nodes, histological grading and ECOG performance status had a prognostic impact on OS.

The optimal cut-off number of lymph nodes with the highest sensitivity and specificity for estimating the outcome was set at 10 after ROC curve analysis.

Removing 10 lymph nodes in our study represents a cut-off with a significant prognostic impact, in particular in resected stage II NSCLC.

Conclusions. Similarly to other cancer (i.e. colorectal cancer), our results suggest that an adequate classification of NSCLC should always include an adequate lymph nodes clearance with a minimum of 10, in particular in stage II NSCLC. The number of resected lymph nodes also could be useful in order to select patients to receive post-operative treatment (radiotherapy ± chemotherapy) for NSCLC.

D15 PRIMARY PLEUROPULMONARY SYNOVIAL SARCOMA: A RETROSPECTIVE CLINICO-PATHOLOGIC STUDY OF 21 CASES FOLLOWED AT THE INSTITUT GUSTAVE ROUSSY (IGR)

Giaj Levra M.[1], Domont J.[2], Blesius A.[2], Cioffi A.[2], Bonvalot S.[2], Le Pechoux C.[2], Boulet B.[2], Novello S.[1], Le Cesne A.[2]

[1]Dipartimento di Scienze Cliniche e Biologiche, Università degli Studi di Torino, AOU San Luigi Gonzaga, Orbassano, Italia; [2]Institut Gustave Roussy, Villejuif, France

Introduction. Primary pleuropulmonary synovial sarcoma (PPSS) is a rare neoplasm well described in literature over the last years. The discovery of the pathognomonic t (x;18) chromosomal translocation has enabled the diagnosis of an increasing number of these tumours.

Patients and methods. This is a retrospective study of 21 consecutive patients (pts) with a diagnosis of primary PPSS treated or followed at the IGR from 1998 to 2010.

Results. Male/female ratio was 11/10, the median age 46 (range 16-72) with a median PS of 0 (1-2). Most common symptoms were asthenia and cough, in 4 cases the diagnosis was accidental. Tumours were localized in 12 cases in the lung, 6 were pleural, 2 mediastinal and in one case carinal. Six patients had synchronous metastases at diagnosis. Sixteen surgical interventions were performed: 11 lobectomies, 3 pneumonectomies, 1 atypical resection and 1 tracheal resection. A R0 resection has been achieved in 68.8% of the cases. Seven pts received a doxorubicin-containing chemotherapy (CT) regimen in adjuvant setting and only four underwent radiotherapy. Thirteen cases of relapse were observed with a median time of 15.7 months (range 4.7-59.7 months) and in 9 cases it was thoracic. Sixteen patients received a palliative chemotherapy. Seventeen (81%) died within 1 month to 73 months (mean 25 months), and 15 patients died within 5 years (71.4%). Three (14.3%) were alive and had no evidence of disease, and 1 patients was alive with evidence of disease. Most of the PPSS were monophasic (76.2%) and the research of chromosomal translocation was available in 15 cases: six were positive for the t (x;18) translocation, four for the fusion gene SSX1 or SYS-SX2, three negative.

Conclusion. PPSS is a rare subset of intrathoracic sarcoma, its clinical features suggest a more aggressive behavior than the synovialsarcoma of other counterparts, possibly related to the difficulty in obtaining adequate surgical margins. Adjuvant (and neoadjuvant) therapies have to be discussed in multidisciplinary committee and proposed in this unfavorable disease.

D16 MDM2 309 SINGLE NUCLEOTIDE POLYMORPHISMS (SNP) AND CLINICAL OUTCOME IN PATIENTS WITH LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF HEAD AND NECK (LASCCHN)

Vivenza D.[1a], Gasco M.[1b], Natoli G.[1b], Monteverde M.[1a], Lattanzio L.[1a], Colantonio I.[1b], Miraglio E.[1b], Comino A.[2], Syed N.[3], Crook T.[3], Merlano M.[1b], Lo Nigro C.[1a]

[1a]Laboratory of Translational Oncology, [1b]Medical Oncology, Oncology Department, [2]Pathology Department, S. Croce General Hospital, Cuneo, Italy; [3]Charing Cross Hospital, Imperial College, London, UK

Background. Disruptive TP53 alterations have been associated with decreased survival in patients with SCCHN. A T >G polymorphism in the promoter region of Mouse Double Minute 2 homologue (MDM2) has been associated with higher MDM2 mRNA and protein levels. Overexpression of MDM2 is thought to interfere with p53-mediated apoptosis and growth inhibition. We hypothesized that the MDM2 containing the G allele (GT or GG genotype) may be associated with worse survival in SCCHN patients (pts).

Methods. We directly sequenced the MDM2 polymorphism on both strands. We then evaluated the correlations between MDM2 polymorphism status and overall survival (OS) in 105 pts affected by LASCCHN. Median follow-up was 39 months. All pts received cisplatin-based chemo-radiotherapy in our department between September 1997 and May 2009. The Kaplan-Meier method and Log-rank test were used to compare survival according to MDM2 polymorphism status. Cox proportional hazards model was used to calculate hazard ratio (HR) adjusted for possible confounding variables, with 95% confidence interval (95% CI).

Results. Median age was 57 years; 85 pts (80%) were male and 94 pts (90%) were stage IV. The genotype frequencies for the MDM2 polymorphism were: T/T 42 (40%), T/G 42 (40%), G/G 21 (20%). Median overall survival (OS) was significantly shorter in patients with genotypes containing the G allele (GT + GG) compared to those with TT genotype (22 months vs 107 months; Log-rank $p < 0.0001$); in addition 5-year survival rates were 8/63 vs 21/42 (Chi square Yates $p = 0.004$). The G allele maintains its effect on survival after adjusting for age, gender, stage, primary site and performance status (HR for death 3.05; 95% CI 1.80-5.19; $p < 0.0001$).

Conclusions. Our findings support the hypothesis that MDM2 SNP309 polymorphism is an independent survival determinant

among advanced stage SCCHN patients treated with cisplatin-based chemo-radiotherapy.

D17 mRNA LEVELS OF GENES INVOLVED IN THE NUCLEAR FACTOR κB (NFkB) AND NOTCH SIGNALLING PATHWAYS IN STAGE IV NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS

Santarpia M.[1,2], Costa C.[2], Pitini V.[1], Sanchez-Ronco M.[3], Magri I.[2], Molina-Vila M.A.[2], Taron M.[2,4], Rosell R.[2,4], Altavilla G.[1]

[1]Human Pathology Department, Medical Oncology Unit, University of Messina, Italy; [2]Pangaea Biotech, USP Dexeus University Institute, Barcelona, Spain; [3]University of Alcala de Henares, Madrid, Spain; [4]Catalan Institute of Oncology, Hospital Germans Trias i Pujol, Badalona, Spain

Background. Little is known about the potential clinical impact of genetic alterations in the NFκB and Notch pathways on NSCLC pts. NFκB pathway is involved in many cellular processes including immunity, inflammation, cell proliferation, survival and migration. NFκB transcription factor is activated by EGFR pathway and KRAS mutations. Musashi 2 activates HES-1 in the Notch pathway, and HES-1 can abrogate CYLD. A20, AEG-1, EZH2 and TRAF6 are also involved in NFκB activation. BRCA1 and RAP80 are modulators of cisplatin-based chemotherapy. Mutations in NFKBIA and DUSP22, which prevent NFκB activation, were described in the sequencing exome of a single NSCLC pt, together with K-ras mutations.

Methods. mRNA expression of Musashi 2, CYLD, HES-1, A20, EZH2, AEG-1, TRAF6, NFKBIA, RelA, BRCA1 and RAP80 was analyzed by quantitative RT-PCR in tumour samples from 60 advanced NSCLC pts. Expression levels by terciles were correlated with clinical characteristics and outcome to chemotherapy. Mutations in NFKBIA and DUSP22 were also assessed by sequencing in a 30 p and 12 cancer cell lines.

Results. Patients characteristics: 36 male; 39 adenocarcinomas; 22 smokers; 23 bone metastases; 9 EGFR mutations; 10 K-ras mutations. No NFKBIA or DUSP22 mutations were observed in any of the pts or cell lines. PFS was 12.3 months (m) for pts in the lowest tercile of AEG-1 expression vs 9.3 m for pts in the intermediate tercile and 4.8 for pts in the highest tercile ($p = 0.002$). Expression levels of the other genes did not correlate with outcome. However, we had previously generated a two-gene risk model based on AEG-1 and BRCA1 expression: pts with high levels of both genes are considered high-risk, pts with low levels of both genes are low-risk, and pts with high levels of one and low levels of the other gene are intermediate-risk. In the present study, PFS was 13.02 months, compared to 5.4 months in those with high levels of both genes and 7.7 months for those with other combinations ($p = 0.025$). The multivariate analysis for PFS confirmed the prognostic role of high BRCA1/AEG-1 expression (HR, 3.1; $p = 0.01$).

Conclusions. NSCLCs have variegated gene expression. AEG-1 and BRCA1 mRNA expression is a genetic signature that can be used as a prognostic model for the management of NSCLC patients.

D18 MUTATION ANALYSIS APPLIED TO CYTOLOGICAL SAMPLES OF LUNG AND COLORECTAL CANCER

Bozzetti C.[1], Naldi N.[1], Nizzoli R.[1], Bortesi B.[1], Zobbi V.[1], Azzoni C.[2], Negri F.V.[1], Tiseo M.[1], Camisa R.[1], Silini E.M.[2], Ardizzoni A.[1]

[1]Medical Oncology Unit, Azienda Ospedaliero-Universitaria, Parma, Italy; [2]Surgical Pathology Unit, Azienda Ospedaliero-Universitaria and COMT (Centro di Oncologia Molecolare Traslazionale) Università, Parma, Italy

Background. Fine needle aspiration (FNA) has become the modality of choice for tissue sampling of many malignancies, providing a remarkable opportunity for both diagnosis and genomic profiling of cancer tissue. In this series, *EGFR* and *Kras* mutational analysis was performed on cytological samples obtained by FNA from 47 tumour lesions (28 non-small cell lung cancers (NSCLC) and 19 distant metastatic lesions of colorectal cancer (CRC)).

Materials and methods. Gene mutations were analyzed on DNA extracted from the cell suspensions obtained by washing the needle in 0.9% sodium chlorite in order to recover the cellular material after smearing on slides for routine cytology. Alternatively, tumour cells scraped from a destained cytological smear were submitted to the mutational analysis. Amplification of exons 18-21 of *EGFR* gene and of exon 2 of *Kras* was performed and PCR fragments were sequenced and analyzed in both forward and reverse directions.

Results. Seventeen of the 28 NSCLCs samples were obtained from the pulmonary mass by transthoracic needle aspiration, 5 from mediastinal lymph nodes by transbronchial needle aspiration, and 6 from superficial metastatic lesions by FNA. The feasibility of both *EGFR* and *Kras* mutational analysis was 93% (26/28). *EGFR* and *Kras* mutations, tested for each NSCLC lesion on both cell suspension and scraped smear, were found in 7 and 7 respectively of the 26 cases. The feasibility of *Kras* mutational analysis on FNAs from distant CRC metastases was 95% (18/19). *Kras* mutations were found in 7/18 metastases sampled by ultrasound-guided FNA. This result was confirmed on archival tissue sections of corresponding primary tumours where *Kras* mutations were found in 9/18 cases. Fifteen/17 (88%) matched cases were concordant (Kappa coefficient = 0.761; $p < 0.001$), 2 cases showing *Kras* mutation in the primary tumour and being negative in the metastasis.

Conclusion. Our findings demonstrate that the cytological samples represent a reliable material for the molecular characterization of tumour lesions whenever surgery is not indicated.

D19 EVALUATION OF CTL ANTIGEN 4 (CTLA-4) EXPRESSION AS PROGNOSTIC FACTOR IN NON-SMALL CELL LUNG CANCER (NSCLC)

Rijavec E., Barletta G., Genova C., Salvi S., Merlo D.F., Margallo E., Boccardo S., Morabito A., Laurent S., Mora M., Ratto G.B., Pronzato P., Truini M., Pistillo M.P., Grossi F.

Istituto Nazionale per la Ricerca sul Cancro, Genova

Background. CTLA-4, a close homologue to CD28, is a vital negative regulator of T-cell activation and proliferation. We previously reported that CTLA-4 is expressed by NSCLC cell lines providing evidence of its involvement in apoptosis induction upon engagement with soluble CTLA-4 ligands (Contardi E, Int J

Cancer, 2005). The present study examined the expression of CTLA-4 on tumour tissues of patients (pts) with radically resected stage I-IIIA NSCLC.

Methods. Tumour tissue samples from 82 pts who underwent surgery between 7/2005-3/2007 were analyzed for expression of CTLA-4 using immunohistochemistry (IHC). Viable tumour was sampled in triplicate for tissue microarray analysis, and slides were stained by IHC with 14D3 mAb (eBioscence, San Diego, CA, USA). All tissue arrays were independently scored by two observers (M.T. and S.S.), blinded to the patients. CTLA-4 score was calculated using the following formula: (1 + I) x PC, where I is the staining intensity and PC the percentage of tumour cells that stained at each intensity, respectively. The score median value was *a priori* chosen as the cut-off point for classifying tumours as CTLA-4-negative (score ≤20) and positive (>20).

Results. The median follow-up time was 41 months (range 28-54), and 27 deaths were observed. CTLA-4 expression was positive in 48% of tumours and similar in males and females (47 vs 47%), age ≤70 and >70 (46 vs 49%), ex-never smokers and current smokers (46 vs 47%), whereas was higher in non-squamous than in squamous carcinoma (53 vs 36%). Cox's multiple regression analysis identified stage and CTLA-4 expression as the only variables associated with survival. The hazard ratio (HR) was 2.76, (95% CI 0.9-8.3; p = 0.07) and 6.61 (95% CI 2.6-16.8; p ≤0.001) for tumour stage II and III compared to stage I respectively, and 0.39 (95% CI 0.2-0.9; p = 0.03) for CTLA-4 score >20.

Conclusions. Our results demonstrate an association between CTLA-4 expression and increased overall survival in NSCLC pts suggesting a prognostic role for CTLA-4 in NSCLC. An increased CTLA-4 expression may contribute to NSCLC progression by modulating the interaction of microscopic disease with CTLA-4 ligand-expressing cells leading to NSCLC cell death.

D20 P95HER2 TRUNCATED FORM AND HER2 GENE COPY NUMBER IN RESECTED NON-SMALL CELL LUNG CANCER (NSCLC)

D'Incecco A.[1], Sacconi A.[2], Alì G.[3], Incarbone M.[4], Terracciano L.[5], Destro A.[6], Roncalli M.[6], Fontanini G.[3], Marchetti A.[7], Varella-Garcia M.[8], Cappuzzo F.[1]

[1]Istituto Toscano Tumori, Oncologia medica, Ospedale Civile, Livorno, Italy; [2]National Cancer Institute Regina Elena, Roma, Italy; [3]University of Pisa, Pisa, Italy; [4]Thoracic Surgery, Ospedale S. Giuseppe Milano and IRCCS Multimedica Sesto S.G., Italy; [5]University Hospital, Division of Molecular Pathology, Basel, Switzerland; [6]University of Milan School of Medicine, Department of Pathology, IRCCS Istituto Clinico Humanitas, Rozzano, Italy; [7]Chieti University, Chieti, Italy; [8]University of Colorado Cancer Center, Aurora, CO, USA

Background. Anti-HER2 therapies failed to demonstrate any benefit in unselected NSCLC. Studies in breast cancer showed that the NH_2-terminally truncated form of HER2 (p95HER2) could confer resistance to HER2 monoclonal antibodies (HER2-mab). HER2 gene amplification (GA) is considered a negative prognostic factor in human malignancies. Aim of the present study was to investigate the role of p95HER2 and HER2 gene copy number (GCN) in NSCLC.

Methods. The study was conducted in a cohort of 447 surgically resected NSCLC with known MET and EGFR GCN status and in 8 additional specimens from NSCLC patients harbouring exon 20 HER2 mutation. Tissue microarray sections were evaluated for p95HER2 by immunofluorescence and for HER2 GCN by fluorescence *in situ* hybridization (FISH).

Results. HER2 GCN was successfully evaluated in 439 patients and increased GCN was found in 60 cases (13.7%), including 22 cases (5.0%) with true GA. HER2 FISH+ status was significantly associated with EGFR (p <0.001) and MET (p = 0.005) GCN. No difference in survival was observed between patients with or without HER2 GA (median 38.0 versus 41.3 months, HR = 0.82; p = 0.47), nor in a context of MET co-amplification (median survival 36.0 versus 20.5 months in MET GA/HER2 GA and MET GA/ HER2-, respectively, HR = 1.29; p = 0.26). P95HER2 was evaluated in 431 patients and the result was positive in 33 cases (7.7%). No association was detected between P95HER2 positive and HER2 increased GCN; interestingly, p95HER2 positive status was more frequently observed in non adenocarcinoma histology (p = 0.001). Among the 22 patients with HER2 GA and among the 8 patients with HER2 mutation, only one resulted P95HER2 positive. In the whole population, p95HER2+ patients had a not significant higher risk of death than p95HER2- (33.0 versus 41.3 months, HR = 1.41; p = 0.22).

Conclusion. HER2 is not prognostic in NSCLC even in a context of MET co-amplification. Although p95HER2 is present in NSCLC, it is unlikely that this event is responsible for the lack of efficacy of HER2-mab therapies observed in clinical trials.

D21 A NEW BAYESIAN SCORING SYSTEM CALCULATOR (BSSC) FOR THE ESTIMATION OF THE PROBABILITY OF MALIGNANCY (EPM) FOR SOLITARY PULMONARY NODULES (SPNS): FEASIBILITY AND PRELIMINARY RESULTS OF A RETROSPECTIVE SERIES

Cingarlini S.[1], Soardi G.A.[2], Ortolani S.[1], Bria E.[1], Cetto G.L.[4], Santo A.[3], Perandini S.[2], Tortora G.[1]

[1]U.O.C. Oncologia Medica dU, Azienda Ospedaliera Universitaria Integrata, Verona, Italy; [2]Radiologia, Azienda Ospedaliera Universitaria Integrata, Verona, Italy; [3]U.O.C. Oncologia Medica, Ospedale Civile Maggiore, Azienda Ospedaliera Universitaria Integrata, Verona, Italy; [4]U.O.C Medicina ad Indirizzo Palliativo, Verona, Italy

Introduction. The treatment decision for incidentally detected SPNs represents a relevant clinical issue for clinical practice. Bayesian analysis may be considered a validated method merging clinical/radiographic characteristics to derive a quantitative EPM. The purpose of the study presented herein is to improve the accuracy of this method in order to build up a tailored diagnostic-therapeutic algorithm.

Materials and methods. The retrospective analysis of subjects referring to Radiology Department of Verona between January 2002 and December 2010 for diseases other than lung nodules represents the 1st step (feasibility study) of the current study. CT scan volumes were acquired by means of a multi-slice 4-row scanner (Volume Zoom, Siemens, Germany) until 2008 and by means of a 64-row scanner (Light Speed 64, General Electrics, USA, feat. Lung VCAR) till present. A BSSC was developed on the basis of clinical parameters (age, smoking history, previous cancer, hemoptysis) and 1st level radiological findings (size, location, shape), by assuming their likelihood ratios according to

screening and meta-analyses data. Contrast enhancement (CE) and minimum focal density (MFD) were considered to improve the accuracy of the calculator; the other online available BSSC (Gurney) was concurrently tested. The prospective multi-institutional external validation (2nd step) will follow.

Results. From 531 identified SPNs, 225 SPNs in 210 patients were selected; exclusion criteria were: more than 3 nodules in the same patient and absence of definitive diagnosis derived either from histological sample or from biological behavior. Accuracy data are shown in the table:

Parameter	Cut-off (HU)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
CE	15 HU	90	45	62	82
	40 HU	69	82	79	73
MFD	-40 HU	87	20	52	61
	-50 HU	97	15	53	83

The high risk population has been assessed as follows: 1) no follow-up if EPM <50%; 2) CT follow-up (with VDT evaluation) if 50% ≤EPM <80%; 3) invasive diagnosis/surgery if EPM ≥80%. Our calculator demonstrated to be more sensitive (FN rate: 10.7% vs 25%) and just little less specific (FP rate: 10% vs 7.5%) when compared to the Gurney SS.

Conclusions. The developed BSSC demonstrated to be accurate in predicting the EPM of SPNs; the external prospective validation is currently ongoing. The adoption of such method may represent a useful tool for clinical practice and a challenging perspective for the early detection of lung cancer.

D22 META-ANALYSIS OF PHASE III TRIALS OF NEOADJUVANT CHEMOTHERAPY FOLLOWED BY SURGERY VERSUS SURGERY ALONE IN STAGE III NON-SMALL CELL LUNG CANCER

Barbieri V., Ciliberto D., Lacaria M., Codispoti S., Marvaso G., Tassone P., Tagliaferri P.

Fondazione per la Ricerca e Cura dei Tumori "Tommaso Campanella" e Università "Magna Graecia", Catanzaro

Introduction. The use of neo-adjuvant chemotherapy in non-small cell lung cancer (NSCLC) has been investigated in the last 20 years in many prospective trials and several meta-analyses have been published. However, few randomized controlled trials have been designed specifically for the stage IIIA disease. We have performed a systematic review and meta-analysis on the efficacy of neo-adjuvant chemotherapy (CT) in this specific setting.

Methods. Randomized phase III clinical trials (RCTs) were considered if they enrolled only stage IIIA patients, included analysis of effects on overall survival (OS) and were published in English as an article or major meeting abstract (time frame 1990-2010). Studies including radiotherapy (RT) or RT/CT combinations were not considered. Meta-analysis was performed by a random effect model approach.

Results. On a total of twelve phase III RCTs, only four studies were identified as specifically enrolling only stage IIIA patients. One study did not contain sufficient data for analysis. The individual HRs for OS were extracted from three eligible studies. The combined analysis suggested a small non significant benefit of neo-adjuvant chemotherapy HR of 0.74 (95% CI 0.45 to 1.21; p = 0.228). The analysis for resection rate demonstrated a significant benefit for combined treatment with an odds ratio (OR) of 0.50 (95% CI from 0.31 to 0.81; p = 0.0046). If R0 resection rate was considered the small benefit of combined treatment, OR: 0.85 (95% CI 0.58 to 1.24) was no more significant (p = 0.4031).

Conclusions. Our meta-analysis from a systematic review of current available phase III RCTs for neo-adjuvant CT followed by surgery in stage IIIA NSCLC failed to demonstrate a significant advantage *versus* surgery alone in terms of OS or R0 resection rate with a small but significant benefit in overall resectability. Novel trials are eagerly awaited which should be based on last generation CT on the the new UICC 7 staging in order to allow an evidence based decision making in this specific setting.

D23 IGF1R AND SRC EXPRESSION AND CO-EXPRESSION AND CO-ACTIVATION IN NON-SMALL CELL LUNG CANCER (NSCLC)

Monica V., Volante M., Lo Iacono M., Ceppi P., Longo M., Capelletto E., Novello S., Scagliotti G.V., Papotti M.

University of Turin, Department of Clinical & Biological Sciences, San Luigi Hospital, Orbassano (Turin), Italy

The insulin-like growth factor type I receptor (IGF1R) is a tyrosine kinase receptor which regulates cell growth, differentiation, survival, transformation and metastasis. Its over-expression and gene amplification have been demonstrated in non-small cell lung cancer (NSCLC) with special reference to the squamous histology. Tyrosine kinase inhibitors and monoclonal antibodies showed promising blocking effects of IGF1R in pre-clinical studies. The tyrosine kinase c-SRC is a signaling transducer of different TK receptors and is highly expressed in lung cancer tissues and cell lines. We tested in four NSCLC cells the effect of figitumumab, a monoclonal antibody against IGF1R in association with a potent c-Src inhibitor, dasatinib, and, in parallel, we analyzed the presence of a putative IGF1R-SRC activated pathway in a series of consecutive surgical NSCLC tissues.

After 72 hours of treatment, both figitumumab and dasatinib alone showed a moderate activity in all cell lines, the former with a mild superior effect in H1299 and Calu-1, compared to A549 and H520 cell lines. At the same time, the simultaneous administration of the two agents resulted in a synergistic increase of cell proliferation blockage in three out four cell lines, H1299, Calu-1 and A549 cells, whereas a strong antagonistic effect was observed in H520 cells. Apoptotic assays showed that both drugs, administered as single agent, induce modest pro-apoptotic effects while a higher rate of apoptotic cells was found with the dasatinib/figitumumab combination in both H1299 and Calu-1 cells.

IGF1R and SRC mRNA tissue expression analyses showed higher IGF1R tumour expression and modulation (normal/tumour expression) in squamous compared to non-squamous histotypes. A strong linear correlation between IGF1R and SRC mRNA expression levels was detected, confirmed by immunohistochemical analysis on the phosphorylated forms of IGF1R and SRC proteins.

In conclusion, our *in vitro* and tumour tissue data preliminarily support the combined inhibition of IGF1R and SRC as a novel therapeutic strategy for a subset of NSCLC patients with a functionally activated status of the IGF1R-SRC pathway.

D24 EFFICACY OF EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) TYROSINE KINASE INHIBITORS (TKIs) IN PATIENTS WITH NON-SMALL CELL LUNG CANCER (NSCLC) WITH BRAIN METASTASES (BM)

La Spina C.M., Beretta G.D., Ripa C., Salvini P., Squadroni M., Stinco S., Ceresoli G.L.

Humanitas Gavazzeni, Bergamo

Background. BM are a common occurrence in patients with NSCLC. Standard treatment options include whole brain radiotherapy (RT) and in selected cases, surgery or stereotactic radiosurgery. The TKIs gefitinib and erlotinib have been approved for advanced NSCLC. We evaluated their efficacy in patients with BM from NSCLC.

Patients and methods. A retrospective analysis of 66 patients with metastatic NSCLC (adenocarcinoma), treated by EGFR TKIs from April 2008 until May 2011, was performed in a single center. BM were diagnosed in 14 patients, 7 synchronous, 7 metachronous. There were 9 females and 5 males, with median age of 59 years. Most patients (71%) had ECOG PS 1. Nine were ex-smokers, 4 never-smokers and one current smoker. The majority (61%) were treated with EGFR TKI after two lines of chemotherapy. Nine were pretreated with RT and two received RT after failure of TKIs treatment; 10 (71%) had no neurological symptoms. In 5 patients only EGFR mutation status was available, positive in two cases. Patients received gefitinib 250 mg (14%) or erlotinib 150 mg (86%), until disease progression or unacceptable toxicity. Chest and abdominal computed tomography (CT) scan and CT or magnetic resonance imaging of brain were performed at baseline and every 2 months.

Results. Among 14 patients, 4 achieved a PR while 4 experienced SD and 6 PD, yielding a disease control rate of 57%. Median duration of response of BM was 6.7 months and median overall survival was 7.4 months. Among 4 responders, all had no neurological symptoms, 3 were males, 2 ex-smokers, one never-smoker and one smoker, and in 2 EGFR mutation was present. Patients with EGFR mutations received EGFR-TKIs as upfront therapy for their BM.

Conclusions. EGFR-TKIs are effective in selected patients with asymptomatic BM from NSCLC and should be considered when clinical characteristics (gender, histology, smoker-status) suggest a high chance of response. In patients with BM at diagnosis and EGRF mutations, TKIs should be administered as upfront therapy.

D25 ELECTROCHEMOTHERAPY FOR THE TREATMENT OF RECURRENT HEAD AND NECK CANCER: PRELIMINARY RESULTS

Porta C., Occhini A., Paglino C., Mevio N., Bertino G., Paulli M., Massaro P., Corbella F., Pedrazzoli P., Benazzo M.

Gruppo multidisciplinare neoplasie del distretto cervico-cefalico, Fondazione IRCCS, Policlinico S. Matteo, Pavia

Background and aim. Electrochemotherapy (ECT) is a tumour ablation modality providing delivery into cell interior of poorly permeant or not permeant chemotherapeutic drugs such as cisplatin and bleomycin. A locally applied electrical field enhances the membrane permeability allowing intracellular accumulation of the chemotherapeutic agent. Aim of the study was to evaluate the effectiveness of ECT for the treatment of patients with recurrent head and neck (H&N) cancer.

Patients and methods. Between April 2009 and January 2011, 15 patients with H&N cancer (13 squamocellular carcinoma, 1 basaloid carcinoma and 1 Merkel cells carcinoma) not suitable for conventional therapeutic options were treated with ECT. Electrical pulses were delivered to 33 lesions (3 primary tumours, 30 recurrences) after an intravenous bolus injection of bleomycin (15000 IU/m^2). In 3 cases the lesion treated was a metastatic lymph node.

Results. Among 31 evaluable lesions, 19 (61.5%) and 10 (32.5%) showed complete or partial response, respectively, for an overall response rate of 94%. All lesions undergoing complete regression were less than 3 cm in their maximum diameter. After a follow-up period ranging from 2 to 20 months 79% of patients are alive (29% disease-free), while 21% have died for either disease progression (14%) or other causes (7%).

Conclusion. Our study confirms that ECT can provide a clinical benefit in patients with recurrent or locally advanced H&N cancer not suitable for conventional therapy. A prospective study is ongoing to better define the role of this therapeutic modality.

D26 INSULIN-LIKE GROWTH FACTOR RECEPTOR 1 (IGF1R) AND EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) AMPLIFICATION AND EXPRESSION IN SURGICALLY RESECTED NSCLC

Flacco A.[1], Ludovini V.[1], Bianconi F.[2], Tofanetti F.R.[1], Ragusa M.[3], Vannucci J.[3], Bellezza G.[4], Mameli M.G.[4], Chiari R.[1], Minotti V.[1], Pistola L.[1], Siggillino A.[1], Baldelli E.[1], Sidoni A.[4], Puma F.[3], Varella-Garcia M.[5], Crinò L.[1]

[1]Medical Oncology Department, S. Maria della Misericordia Hospital, Perugia, Italy; [2]Department of Electronic and Information Engineering, [3]Department of Thoracic Surgery, [4]Institute of Pathological Anatomy and Histology, University of Perugia, Perugia, Italy; [5]Department of Medicine/Medical Oncology, University of Colorado Cancer Center, Aurora, CO

Background. IGF1R represents a novel molecular target in non-small cell lung cancer (NSCLC). IGF1R and EGFR activation is essential to mediate tumour cell survival, proliferation and invasion. This study investigates the prognostic role of *IGF1R* and *EGFR* copy number gain (CNG) by fluorescence *in situ* hybridization (FISH) and protein overexpression by immunohistochemistry (IHC) in surgically resected NSCLC.

Methods. 114 NSCLC patients were evaluated; median age was 66 years (range 40-84), male/female: 96/18; squamous (SCC)/adeno/BAC/other: 59/34/9/12; smoker/never smoker: 105/9, and stage I/II/III: 71/18/25. *IGF1R* and *EGFR* FISH were tested by customized and commercial probes, respectively; positive specimens showed gene amplification or polysomy (≥4 copies in ≥10% of tumour cells). IGF1R and EGFR protein expression were evaluated using mouse antibodies (clones 24-31 and 3147, respectively); overexpression was defined by ≥10% positive cells. Kaplan-Meier estimates of survival and time to recurrence were calculated for clinical and biologic variables using Cox model for multivariate analysis.

Results. Forty-six tumours (40%) were *IGF1R* FISH+ and 76 (77%) were *EGFR* FISH+. *IGF1R* FISH+ was associated with *EGFR* FISH+ (p = 0.03) and co-amplification was observed in 34 cases (30%). *IGF1R* and *EGFR* FISH+ were associated with SCC (p = 0.01 and p = 0.05, respectively). IGF1R and EGFR overexpression was detected in 36% and 55% of NSCLC patients and co-expression was detected in 25%. Co-amplification and co-expression of both receptors were significantly associated (p = 0.045). IGF1R and EGFR co-amplification and co-expression associated with shorter disease-free survival (DFS; p = 0.05, p = 0.05 respectively), also at multivariate analysis adjusting for stage (p = 0.0002).

Conclusions. *IGF1R* and *EGFR* are frequently co-amplified in NSCLC and CNG correlates with protein overexpression. Both co-amplification and co-expression of IGF1R and EGFR predict shorter DFS. These results provide a strong rational for targeting simultaneously EGFR and IGF1R in clinical trials for NSCLC.

We thank the Italian Association for Cancer Research (AIRC) for supporting the study (AF Fellowship).

D27 ADVANCED NSCLC TREATMENT: BEYOND THE THIRD-LINE IN THE TARGETED THERAPIES ERA

Gori B.[1], Caffo O.[2], Ricciardi S.[1], Longo F.[3], Intagliata S.[4], Fulvi A.[1], Del Signore E.[1], Di Salvia M.[1], Belli R.[1], Migliorino M.R.[1], de Marinis F.[1]

[1]Oncological Pulmonary 1st Unit, San Camillo Hospital, Rome, Italy; [2]Department of Medical Oncology, Santa Chiara Hospital, Trento, Italy; [3]Department of Medical Oncology, Umberto I Hospital, Rome, Italy; [4]Department of Medical Oncology, University Campus Bio-Medico, Rome, Italy

Introduction. In advanced non-small cell lung cancer (A-NSCLC) systemic therapy may relieve symptoms and prolong survival. No valid data exists on the effectiveness of therapy beyond third-line.

Methods. We analyzed 152 patients in an observational retrospective study (from 2001 to July 2010) with A-NSCLC, who received at least a third-line treatment after a platinum-based first-line. The aim of the study was to evaluate the possible correlation between main prognostic factors and prolonged multiline treatment.

Results. Patients were predominantly males (62%), all Caucasians, with a median age at diagnosis of 61 years (33-76), all with an ECOG PS 0-1 and stage IIIB/IV (40/112).

We found adenocarcinoma in 75% of patients, squamous cell carcinoma in 14% and NOS hystologies in 11%. 22% were never smokers, 13% current smokers and 65% former smokers. 13 pts of 53 pts analyzed (24%) expressed an EGFR mutation. All pts received a platinum based first-line treatment, 16% received a maintenance therapy after first-line, 37% received a fourth-line, 14% a fifth-line. 11/13 mutated patients received an oral TKI as second-line treatment (considering the remboursement approval time in Italy from AIFA), while only two patients received erlotinib as third-line. The median OS of all the population was 26 months (6-83), while the median PFS between first- and second-line or between second- and third-line are respectively 7 (2-14) and 5 months (1-48).

The median OS of EGFR mutated pts was 24 months (10-72) with median PFS between first- and second-line, second and third-line and third- and fourth-line respectively of 6 months (2-12), 11 months (8-40) and 3 months (1-14). The final results with a multivariate analysis are ongoing.

Conclusions. In our population we report a significant advantage in median OS (26 months) toward the historical OS reported in literature. In the 100 pts not molecularly investigated we cannot exclude harboring of EGFR mutations. The final data will be presented at the AIOM Congress.

D28 BALANCING THE TOXICITIES OF THE COMBINATION OF PLATINUM COMPOUNDS PLUS IRINOTECAN (CPT-11) OR ETOPOSIDE (VP-16) FOR THE TREATMENT OF EXTENDED SMALL-CELL LUNG CANCER (E-SCLC): META-ANALYSIS OF RANDOMIZED CLINICAL TRIALS (RCTS)

Pappagallo G.[1], Grossi F.[2], Massari F.[3], Barletta G.[2], Milella M.[4], Rijavec E.[2], Cingarlini S.[3], Genova C.[2], Tortora G.[3], Bria E.[3]

[1]Epidemiologia-Sperimentazioni Cliniche, Ospedale Civile, Mirano (VE); [2]Lung Cancer Unit, National Institute for Cancer Research, Genova Italy; [3]U.O.C. Oncologia Medica dU, Azienda Ospedaliera Universitaria Integrata, Verona, Italy; [4]Medical Oncology, Regina Elena National Cancer Institute, Roma, Italy

Background. In absence of significant advances for the systemic treatment of E-SCLC in the last 20 years, the addition of CPT-11 to platinum compounds (CIS or CARBO) represents one of the small attempts to progress over the standard treatment with CIS/CARBO plus VP-16. In addition to the relatively small benefits provided, concerns exist with regard to the safety profile of such comparison. To address this issue, a literature-based meta-analysis was conducted.

Methods. Hazard ratios (HR) with 95% confidence intervals (CI) were extracted and cumulated according to a random-effect model from papers or presentation. Differences in overall survival (OS) and progression-free survival (PFS) were explored. Overall response rates (ORR), and WHO-grade 3-4 toxicities (documented in at least half of the RCTs) absolute differences (AD) with 95% CI were calculated; the number of pts needed to treat in order to harm (NNH) was calculated. A sensitivity analysis for efficacy according to the platinum compound (CIS vs CARBO) was performed as well as testing for heterogeneity.

Results. Six trials (1796 pts) were gathered. Data were available for 5 RCTs for OS (1726 pts) and PFS (1590 pts); patient population ranged from 70 to 641 patients. Both an OS advantage (HR 0.80, 95% CI 0.69-0.92, p = 0.003) and a PFS advantage (HR 0.86, 95% CI 0.72-1.03, p = 0.10) were observed in favour of CPT-11 over VP-16. A significant interaction favouring CBDCA (p = 0.048) was also observed. No significant differences were found in ORR between CPT-11 (52.0%, 95% CI 48.7-55.4) and VP-16 (54.0%, 95% CI 50.5-57.6). Significant differences in toxicity rates (with 95% CI) are shown in the table (see next page).

Conclusions. The addition of CPT-11 to CIS/CARBO seems to determine a slight while significant survival advantage with a different safety profile in comparison with VP-16, by providing significantly lower hematological toxicity, and higher diarrhea and vomiting.

Table - D28

Toxicities (G3-4)		CPT-11 (95% CI)	VP-16 (95% CI)	AD (%)	NNH
Hematologic	Anemia	7.5% (5.9-9.2)	12.6% (10.3-14.8)	-5.1	19
	Neutropenia	37.8% (34.5-41.1)	70.0% (66.7-73.3)	-32.2	3
	Febrile neutropenia	4.0% (2.4-5.6)	10.5% (7.7-13.3)	-6.5	15
	Thrombocytopenia	6.1% (4.5-7.6)	15.8% (13.3-18.2)	-7.7	13
	Leukopenia	18.4% (15.6-21.2)	30.6% (27.3-33.9)	-12.2	8
Non-hematologic	Diarrhea	17.9% (15.4-20.3)	1.5% (0.8-2.3)	+16.4	6
	Vomiting	11.1% (8.8-13.4)	6.7% (4.8-8.7)	+4.4	23

D29 PERITONEAL MESOTHELIOMA. A 12 YEARS SINGLE INSTITUTION EXPERIENCE

Ciuffreda L.[1], Sambuco A.[1], Gangemi M.[2], Mirabelli D.[2], Pazè E.[1]

[1]SC Oncologia 1, A.O.U. S. Giovanni Battista di Torino; [2]SCDU Epidemiologia dei Tumori, Università di Torino e CPO Piemonte

Introduction. Malignant peritoneal mesothelioma (MPM) is a rare disease with poor prognosis. We describe the characteristics, treatments and outcomes of MPM patients admitted at our hospital in the period 1999-2010.

Materials and methods. We did a retrospective search based on clinical charts and electronic files of all MPM patients admitted at our hospital.

Results. Seventy-one patients with MPM were admitted over 12 years. Fifty-three were living in Turin or its province, 11 came from outside Piedmont. Date of diagnosis was not retrieved for one patient living outside Piedmont and therefore he is not included in the survival assessment.

There were 28 females and 43 males. Mean age at diagnosis was 61 years (range 30-82).

MPM was epithelioid in 41 patients, biphasic in 9, sarcomatoid in 3, glandular in 1 and not specified in 17. Eighteen patients had pleural and peritoneal mesothelioma at diagnosis.

Surgery with curative intent was performed in 26 patients (19 with hypertermic intraoperatory chemotherapy); 9 further patients underwent debulking surgery.

Thirty-three patients received i.v. chemotherapy.

Median overall survival (MOS) was 7 months (range 0-138+), and did not differ between peritoneal-only or pleural/peritoneal presentation. MOS was 5.5 months (0-30) among females and 9.5 months (0-138+) among males. Epithelioid MPM had MOS of 8.5 months compared to 5.5 of non-epithelioid. Patients undergoing radical or debulking surgery had MOS of 8.5 months (10 months for radical, 6 months for debulking) compared to 5.5 months of those not operated. Only 5 patients survived longer than 3 years (40, 58, 69, 85 and 138+ months).

Conclusion. MPM patients carry a poor prognosis and few survive longer than 3 years from diagnosis. In our experience surgery with curative intent has been performed in a high percentage of patients (26 of the 52 with peritoneal-only presentation), likely because of availability of good surgical expertise which attracted patients from other regions. Patients undergoing surgery with radical intent may have a longer survival.

D30 INCIDENCE OF DIFFERENT K RAS MUTATION IN NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS, TAILOR STUDY

Martelli O.[1], Rulli E.[2], Bettini A.[3], Farina G.[4], Longo F.[5], Moscetti L.[6], Pavese I.[7], Alabiso O.[8], Bertolini A.[9], Tomirotti M.[10], Farris A.[11], Veronese S.[12], Ferrari V.[12], Marsoni S.[13], Lauricella C.[12], Ganzinelli M.[2], Broggini M.[2], Marabese M.[2], Floriani I.[2], Copreni E.[2], Bertolini A.[14], Pellegrino A.[15], Ardizzoia A.[16], Palmeri S.[17], Gherardi G.[18], Bianchi F.[18], Scanni A.[4], Garassino M.C.[4] on behalf of the TAILOR investigators

[1]Oncology Department, San Giovanni Hospital, Rome, Italy; [2]Oncology Department, Istituto di Ricerche Farmacologiche "Mario Negri", Milan, Italy; [3]Medical Oncology Department, Ospedali Riuniti, Bergamo, Italy; [4]Oncology Department, Fatebenefratelli and Ophtalmic Hospital, Milan, Italy; [5]U.O.C. Oncology A, Policlinico Umberto I, Roma, Italy; [6]Oncology Division, Belcolle Hospital, Viterbo, Italy; [7]Oncology, San Pietro Fatebenefratelli Hospital, Roma, Italy; [8]Oncologia Medica, Azienda Ospedaliera "Maggiore della Carità", Novara, Italy; [9]S.C. Medical Oncology, Ospedale Civile di Sondrio, Sondrio, Italy; [10]U.O. Oncologia Medica Fondazione IRCCS Ca' Granda, Ospedale Maggiore, Policlinico, Milan; [11]Oncologia Università di Sassari; [12]Pathology Department, Ca' Granda Niguarda Hospital, Milan, Italy; [13]Southern Europe New Drug Organization (SENDO), Milano, Italy; [14]S.C. Oncologia Medica, Azienda Ospedaliera Valtellina e Valchiavenna, Presidio Sondrio; [15]Dipartimento di Medicina Sperimentale "Università La Sapienza", Roma; [16]Dipartimento Oncologico Azienda Ospedaliera "Ospedale A. Manzoni" Lecco; [17]Oncologia Medica, Dipartimento di Oncologia, Policlinico Universitario "P. Giaccone", Palermo; [18]U.O.C. Anatomia Patologica, Ospedale Fatebenefratelli e Oftalmico, Milan

The RAS/MAPK pathway, is one of the major signalling network linking epidermal growth factor (EGFR) activation to cell proliferation and survival. Recently evidence reported that genetic K Ras alterations beyond the classical ones could have an important role in human cancer. They suggested that different RAS alleles could be important for selection of the therapy. While K Ras mutations seems to negatively select patients affected by colon cancer, for EGFR inhibitors treatment, their role in non-small cell lung cancer (NSCLC) is still debated. We are conducting a phase III randomised trial (TAILOR, NCT00637910), comparing erlotinib to docetaxel in second-line to evaluate the role of biological features in predicting efficacy to treatment in EGFR non mutated patients. Up to date we have prospectively collected a total of 341 samples of NSCLC patients. In 85 patients out of 341 (24%) a mutation of K Ras was found. Al least nine kinds of mutation were identified according to the replaced basis or aminoacid substitution (G12C 36%, G12V 21%, G12D 16%, G12A 9%, G12S 2%, G13D 6%, G13C 5%, G12R 1% and G12F 1%). In particular, we found that G12C is the most expressed mutation in lung cancer, while in colon cancer, G12D is the most common one. The histology in the patients with K Ras mutation was: 76% adenocarcinoma, 6% squamous, 3% large cell and 2% bronchioloalveolar. The smoker status of the patients with K Ras

mutation was: 38% current smoker, 53% ex-light smoker and 9% never smoker. In the patients were grading (G) was expressed the 60% of the patients with K Ras mutation were G3. This information will be helpful for a correlation with the outcome to the therapy, and the different type of mutation could indicate that the simple definition of K Ras mutated tumour could not be enough without the definition of the specific mutation present to identify patients with a different probability of responding to therapy.

D31 IMPACT OF SINGLE-NUCLEOTIDE POLYMORPHISMS IN GENES CODING FOR FOLATE PATHWAY ENZYMES ON EFFICACY/TOXICITY OF GEMCITABINE AND PEMETREXED BASED THERAPY IN ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC): NEW PROSPECTIVES FOR OLD MARKERS

Toscano G., Franchina T., Briguglio R., Colonese F., Berenato R., Alafaci E., Caristi N., Zanghì M., Scimone A., Ientile R.*, Adamo V.

*Unit of Integrated Therapies in Oncology, Department of Human Pathology, University of Messina, Italy; *Department of Biochemical, Physiological and Nutritional Sciences, University Hospital, Messina*

Background. Several studies suggested associations between polymorphisms in folate pathway genes and alterations in protein expression, that may disclose many genetic influences on cytotoxic drug sensitivity. Gemcitabine and pemetrexed are active antitumour agents, approved for NSCLC. However, there is still a lack of appropriate biomarkers for predicting the therapeutic response and toxicity to these drugs. The aim of this study is to establish the potential predictive role of methylenetetrahydrofolate reductase (MTHFR C677T and A1298C) and thymidylate synthase (TS enhancer region and 3' untranslated region) as new biomarkers for gemcitabine and pemetrexed treatment.

Methods. Genomic DNA was isolated from baseline peripheral blood lymphocytes of 45 pts, using puregene genomic DNA purification system. Clinical and outcome data were collected. Patients (29 M/16 F) median age was 66.1 (range 45-84). Gemcitabine based therapy was performed in 33 patients (pts) and pemetrexed based therapy in 12 pts with a median TTP of 7.2 and 5.5 months respectively. Genotyping for MTHFR polymorphisms was carried out by DG-DGGE (double gradient-denaturing gradient gel electrophoresis) and for TS Promoter Polymorphisms with PCR and subsequent electrophoresis on 3% agarose gel. Patients outcome data were compared with MTHFR SNPs and TS VNTR expression. A multivariate analysis was performed.

Results. We have recorded the longer median TTP in patients treated with gemcitabine, expressing the combined MTHFR CC677/AC1298 genotype (10.4 months) and with TS genotype homozygous for triple repeats (3R/3R) (9.7 months).

In the group treated with pemetrexed the longer TTP was recorded for patients expressing the combined MTHFR CT677/AA1298 genotype (7.7 months). Moreover, all patients with MTHFR TT677/AA1298 genotype obtained progression of disease.

Conclusions. Although they are preliminary, these data support the possible role of MTHFR and TS genotypes as predictive markers in gemcitabine and pemetrexed therapy. Further validation and investigation of the involvement of genotypes of folate metabolizing enzyme are needed to confirm these findings and to evaluate their correlation with chemotherapy metabolism and activity.

D32 SECOND-LINE THERAPY IN PEMETREXED PRETEATED PATIENTS (PTS) WITH MALIGNANT PLEURAL MESOTHELIOMA (MPM): A SINGLE CENTER EXPERIENCE

Stinco S., Beretta G.D., La Spina C.M., Ripa C., Salvini P., Squadroni M., Ceresoli G.L.

Humanitas Gavazzeni, Bergamo

Background. MPM is an aggressive tumour with a dismal prognosis. The combination of pemetrexed with a platinum compound is considered the standard first-line (FL) therapy in unresectable disease. Unfortunately, most pts progress during or after FL treatment, and there is no approved drug or drug combination for second-line (SL). We evaluated the role of SL therapy in a consecutive series of pts progressing after FL pemetrexed-based chemotherapy.

Patients. From January 2009, 24 pts with MPM received a SL treatment in our center. Median age was 64.5 years; 8 were females, 16 males; ECOG performance status was 0 in 14 and 1 in 10 patients. Histology was epithelial in 22, mixed in 2. All pts were pretreated with pemetrexed, as a single agent in 1 case, in combination with carboplatin (15), cisplatin (6), or both carboplatin and bevacizumab (2 pts) in the remaining cases.

Results. Two main groups of pts were identified. Patients with a prolonged (>9 months) progression-free survival (PFS) after FL treatment were retreated with a pemetrexed-based regimen (15 cases), while pts with a shorter PFS after FL received either vinorelbine (7 pts) or an experimental therapy (2 pts). Of note, these latter 2 pts received vinorelbine at progression as third-line. Twenty-one pts are evaluable after SL, in 3 SL therapy is ongoing. Eleven of 13 pts (85%) receiving pemetrexed re-challenge had a disease control, with 9 partial responses (PR) and 2 stable diseases (SD), while disease control was observed in only 2/6 (33%) evaluable pts in the vinorelbine group (2 SD). Median PFS in the two groups were 9.0 months (range 4.3-18.1) and 2.3 months (range 0.7-13.1), respectively.

Conclusions. Re-challenge with a pemetrexed-based regimen is a valuable SL strategy in pts achieving a prolonged PFS after a FL pemetrexed-based chemotherapy. Patients rapidly progressing after FL treatment are better candidates to SL experimental approaches. Treatment with SL vinorelbine seems partially active in a subset of these patients.

D33 LUNG CANCER IN NEVER SMOKERS: A MONO-INSTITUTIONAL EXPERIENCE

Chiari R., Bennati C., Molica C., De Angelis V., Minotti V., Metro G., Ludovini V., Duranti S., Currà M.F., Scafati C., Flacco A., Baldelli E., Crinò L.

Medical Oncology Department, S. Maria della Misericordia Hospital, Perugia, Italy

Introduction. Lung cancer (LC) in never smokers (NS) represents a distinct disease entity. From May 2003 to January 2011, 123 stage IV NS LC patients (pts) were followed at our Institution.

Patients. F/M 73/50 (59.3/40.7%). Median age 61 yrs (range 29-78). All of them had a good PS (ECOG 0-1). Histology: squa-

mous/adenocarcinoma/NoS 9/95/19 (7.3/77.2/15.4%). Number of metastatic sites: single/multiple 57/56 (54.5/45.5%). EGFR mutation (exons 18-21) was performed in 87 pts (70.7%) with 47.1% mutated (mut) and 52.9% wild type (wt). K Ras mutation (exon 2) was studied in 85 pts (69.1%) with 8.2% mut and 91.8% wt. 4/20 (20%) double wt EGFR/K-RAS pts scored positive at FISH for EML4-ALK translocation.

Treatment. 111 pts received first-line chemotherapy (CHT): 102 (91.8%) a platinum doublet and 9 (8.2%) gemcitabine. Ninety-four pts (76.4%) received an EGFR-TKI. Eighty-six pts (77.4%) both CHT and an EGFR-TKI. Sixty-four pts (52%) received at least one further line of CHT (median 2-4). ORR, PFS and OS were evaluated for the overall population (123 pts) as well as for EGFR mut versus wt pts.

Results. ORR to first line CHT was 43.8% (EGFR wt: 52.3% vs EGFR mut: 48.5%).

Ninety out of the 94 treatments with an EGFR-TKI (in 82 pts) were evaluable for response. 69/82 pts had a known EGFR status (24 EGFR wt, 45 EGFR mut). ORR to EGFR-TKIs was 46.3% (EGFR wt: 29.1% vs EGFR mut: 55.5%).

PFS and OS in the overall population were 6.1 and 31.6 months (mo). Median OS for TKI treatment (ever/never) was 35 vs 14.4 mo ($p = 0.002$).

PFS/OS in the 87 pts with a known EGFR status were: all (6.7/40 mo); EGFR wt (6.5/36 mo); EGFR mut (7/43.6 mo). The difference in OS between EGFR mut and wt was statistically significant ($p < 0.09$).

Conclusion. In this group of never smoker lung cancer pts, EGFR mutation positive status confers a survival advantage but it does not predict for better ORR to CHT.

D34 IMPACT OF EARLY NUTRITIONAL SUPPORT ON NUTRITIONAL STATUS IN PATIENTS WITH HEAD AND NECK CANCER RECEIVING (CHEMO-) RADIATION THERAPY

Carandina I., Gilli G., Marzola M., Pizzutilo P., Piva E., Scapoli D., Schirone A., Frassoldati A.

U.O. Oncologia Clinica, Azienda Ospedaliero-Universitaria S. Anna, Ferrara

Background. Maintaining adequate nutritional status is an essential part of the management of patients with head and neck cancer receiving chemo and/or radiation therapy, in order to prevent unplanned breaks, which are associated with worse disease control.

Methods. All patients undergoing (chemo-)radiation therapy for locally advanced head and neck cancer or adjuvant (chemo-) radiation therapy underwent a nutritional evaluation before the beginning of the treatment, in order to pre-plan the best nutritional support for each of them. According to pre-therapy nutritional status, site of the primary, planned therapy and comorbidity, a nutritional team decided for oral supplementation or planned the placement of medical devices (feeding tube or central venous catheter) for delivering artificial nutrition.

Results. Seventy-seven patients were evaluated. The majority received artificial nutrition during the treatment: 28.4% enteral nutrition (EN), 19.4% parenteral nutrition (TPN), 44.8% oral support (oral supplement containing eicosapentaenoic acid or/and progesterone derivates). Effects on nutritional status were evaluated in terms of weight maintenance, body composition and biochemical modifications from baseline. EN seems to guarantee the best results for all variables: weight median variation (-0.45 kg), albumin serum levels median variation (+0.40 ng/dL), prealbumin serum levels median variation (+1.28 mg/dL), transferrin serum levels median variation (+19.00 mg/dL), fat body mass median variation (-1.08 kgL), fat free body mass median variation (+0.40 kg), total body water median variation (-0.52 kg). Furthermore, a trend toward lower incidence of G3-4 mucosite in the EN than in the TPN subgroup (50% vs 66.7% respectively) has been observed, as well as and a trend for shorter duration of mucosite (14.68 ± 19.14 days vs 22.50 ± 21.98 days respectively).

Conclusions. Nutritional support with enteral nutrition during (chemo-)radiotherapy for head and neck cancer seems to guarantee a better outcome in terms of maintenance of nutritional status and treatment tolerance.

D35 INTEGRATED-CARE-PATHWAYS FOR NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS: AVOIDABLE COST ANALYSIS IN A QUALITY IMPROVEMENT PROJECT

Merlo V.[1], Rizzato S.[1], Sibau A.M.[1], Zumerle G.[2], Gaiardo M.[1], Gurrieri L.[1], Macerelli M.[1], Menis J.[1], Tozzi V.[3], Fasola G.[1]

[1]Dipartimento di Oncologia, [2]Controllo di gestione, Azienda Ospedaliero-Universitaria di Udine, Italia; [3]CERGAS (Centre of Research on Health and Social Care Management), Università Bocconi di Milano, Italia

Background. Improving the quality of care (QoC) for NSCLC patients is challenging. Integrated-care-pathways (ICPs) have been proposed as quality improvement strategy to enhance the clinical and organizational efficiency of the existing care process.

Methods. The care process for 175 NSCLC patients referring to the Oncology Department of Udine University Hospital during 2008 has been assessed. A focus group composed by all the professionals involved in the management of NSCLC patients was formed. The focus group identified and tested on the study population 11 QoC indicators and corresponding benchmarks, derived both from previously published studies and from international professional guidelines. In cooperation with the researchers of the Cergas Center, Bocconi University of Milan, the extra costs for inappropriate procedures were estimated by the sums through which the regional health care system funds the hospital.

Results. The gap between current practice and the benchmark objectives has been identified, allowing the quantification of the distance of real pathways from the benchmark standards, also in terms of avoidable costs. The average estimated costs for each in- and outpatient were 6482€ and 1860€, respectively. Overall, the most critical and expansive management was the early disease stages one. Even the follow-up phase seems to be more intensive in terms of visits and procedures than the one suggested by the guidelines. The radiodiagnostic procedures and chemotherapy were the most frequent services delivered: 90% of the total cost (302.549€ out of 336.271€) was due to chemotherapy sessions and brain, chest and abdomen CTs.

Conclusion. Developing a valid set of QoC indicators allows to measure the quality of the care delivered, it is a first step towards improving its appropriateness and reducing the avoidable costs. The extension of this methodology could produce interest-

ing results that should be shared and discussed with the hospital managers in order to guide the redesign of ICPs.

D36 EGFR FASTNET: THE ITALIAN NETWORK FOR EPIDERMAL GROWTH FACTOR RECEPTORS (EGFR) MUTATION ANALYSIS IN NON-SMALL CELL LUNG CANCER (NSCLC)

Normanno N.[1], Pinto C.[2], Taddei G.L.[3], Mari E.[4], Troncone G.[5], Graziano P.[6], Mottolese M.[7], Ludovini V.[8], Zupo S.[9], De Maglio G.[10], Roz E.[11], Russo A.[12], Larocca L.M.[13], Di Maio M.[1], Gambacorta M.[14], Nappi O.[15], Viale G.[16], Ardizzoni A.[17], Crinò L.[18], Perrone F.[1], Marchetti A.[19]

[1]Istituto Nazionale Tumori, Fondazione G. Pascale, Napoli; [2]Policlinico S. Orsola Malpighi, Bologna; [3]Università degli Studi di Firenze; [4]AstraZeneca Italia, Basiglio (MI); [5]Università Federico II, Napoli; [6]Azienda Ospedaliera S. Camillo Forlanini, Roma; [7]Istituto Nazionale Tumori Regina Elena, Roma; [8]Ospedale S. Maria della Misericordia, Perugina; [9]Istituto Nazionale per la Ricerca sul Cancro, Genova; [10]Azienda Ospedaliera Universitaria, Udine; [11]Casa di Cura La Maddalena, Palermo; [12]Policlinico Universitario P. Giaccone, Palermo; [13]Policlinico A. Gemelli, Roma; [14]Ospedale Niguarda Ca'Granda, Milano; [15]Azienda Ospedaliera A. Cardarelli, Napoli; [16]Istituto Europeo di Oncologia, Milano; [17]Azienda Ospedaliera, Parma; [18]Azienda Ospedaliera Silvestrini, Perugia; [19]Università G. d'Annunzio, Chieti

Background. Gefitinib was approved in Italy for the treatment of patients with advanced NSCLC carrying mutant EGFR in May 2010.

Methods. The EGFR FASTnet program was designed to facilitate the exchange of biological material, clinico-pathological data and diagnostic reports between medical oncologists, primary pathologists and referral laboratories through a dedicated website (www.egfrfastnet.it), a call center and a courier. EGFR mutational analysis was carried by Sanger sequencing, Real Time PCR, Pyrosequencing, Fragment Analysis and High resolution melting (HRM). The Italian Association of Medical Oncology (AIOM) and the Italian Society of Surgical Pathology and Cytopathology (SIAPEC-IAP) have full access to the anonymous database of EGFR FASTnet.

Results. The EGFR FASTnet network started in July 2010 and as of March 2011, 355 oncologists, 73 primary pathologists and 27 referral laboratories joined the program. In this period, 1235 patients were enrolled. The cohort of patients was significantly enriched for adenocarcinoma histology (997 [81%]), female sex (465 [38%]) and smoking history (never smoker 324 [26%], former smoker >15 yrs 280 [23%], light smoker 67 [5%]). Mutational analysis was feasible in 1133 pts (92%), on the primary tumour (852 [75%]) or metastases (281 [25%]). At the registration, 59% of the patients had not received yet treatment for advanced disease. Mutational analysis was carried by Sanger sequencing in 732 cases (59%), by real time PCR in 34 cases (3%), by pyrosequencing in 83 cases (7%) and by other techniques in 284 (25%). EGFR mutations were found in 167 cases (14.7%): 104 in exon 19 (62.2%), 53 in exon 21 (31.7%), 3 in exon 18 (1.8%) and 7 in exon 20 (4.2%). Proportion of mutated cases was not significantly different among the techniques: Sanger 15.2%, real time PCR 23.5%, pyrosequencing 10.8%, other 13.7% ($p = 0.33$). A higher mutation rate was found in never smokers (27.9%), former smokers >15 yrs (16.1%) and light smokers (14.3%), as well as in adenocarcinoma (16.0%) and females (24.5%).

Conclusions. The EGFR FASTnet network allows assessment of EGFR mutations in a population of Italian NSCLC patients in centers with or without molecular biology facilities. The patients to be tested for EGFR mutations are spontaneously selected by medical oncologists according to known predictive factors. The results of the mutational analysis from clinical practice are consistent with data from literature.

This program is supported by AstraZeneca Italy.

D37 KRAS AND BRAF MUTATIONAL STATUS PREDICTS THE SENSITIVITY OF THYROID CARCINOMA CELL LINES TO SUNITINIB

Piscazzi A.[1], Fabiano A.[2], Costantino E.[1], Maddalena F.[1], Natalicchio M.I.[3], Antonetti R.[3], Cignarelli M.[2], Landriscina M.[1]

[1]Sezione di Oncologia Medica, [2]Sezione di Endocrinologia, Dipartimento di Scienze Mediche e del Lavoro, Università degli Studi di Foggia; [3]Laboratorio di Biologia Molecolare, Azienda Ospedaliero-Universitaria Ospedali Riuniti, Foggia

The multi-kinase inhibitor sunitinib is currently being evaluated in human advanced thyroid carcinomas, based on the evidence that VEGF and PDGF receptors are valuable molecular targets for the treatment of this malignancy. However, the criteria for the selection of thyroid tumours that may benefit from sunitinib are lacking.

The role of activating mutations of KRAS and BRAF genes on sunitinib antiproliferative activity has been evaluated in a panel of thyroid cancer cell lines at different degrees of differentiation: follicular differentiated thyroid carcinoma ML-1 and WRO cells, harboring wild type KRAS and BRAF genes; papillary differentiated thyroid carcinoma TPC-1 cells, harboring the RET/PTC-1 rearrangement; undifferentiated thyroid carcinoma CAL-62 cells, harboring the G12R KRAS mutation; undifferentiated FRO and BHT-101 thyroid carcinoma cells, harboring the V600E BRAF mutation. Interestingly, a significant inhibition of cell proliferation was observed in KRAS/BRAF wild type ML-1, WRO and TPC-1 cells, whereas KRAS- or BRAF-mutated FRO, BHT-101 and CAL-62 cells exhibited lack of sensitivity to sunitinib. The analysis of the cell cycle showed accumulation of cells in the G0 phase, with a parallel inhibition of the S phase only in sunitinib-sensitive thyroid carcinoma cell lines, without induction of apoptosis. Consistently, sunitinib inhibited the phosphorylation of ERK1/2 in KRAS/BRAF wild type cells, without affecting ERK signaling in KRAS- or BRAF-mutated thyroid carcinoma cells. Of note, the transfection, in KRAS/BRAF wild type WRO cells, of a cDNA encoding for an activated form of KRAS resulted in the inability of sunitinib to inhibit the cell cycle in G0 phase and ERK1/2 phosphorylation. Similarly, the activation of ERK pathway by EGF stimulation resulted in the loss of sensitivity to sunitinib in WRO cells.

These results suggest that human thyroid carcinomas harboring activating mutations of KRAS or BRAF genes may be insensitive to the antiproliferative activity of sunitinib and that these oncogenic mutations deserve to be evaluated as predictive markers of efficacy in thyroid carcinoma treated with sunitinib in clinical trials.

D38 ERLOTINIB EVERY OTHER DAY (EOD): A MULTICENTER OBSERVATIONAL STUDY

Passaro A.[1], Fasano M.[2], Morgillo F.[2], Pellegrino A.[1], Cantile F.[2], Alesini D.[1], Cortesi E.[1], Ciardiello F.[2]

[1]Division of Medical Oncology B, Sapienza University of Rome; [2]Division of Medical Oncology, Department of Clinical and Experimental Medicine and Surgery F. Magrassi and A. Lanzara, Second University of Naples

Background. Erlotinib is a tyrosine kinase inhibitor (TKI) of the EGFR that is involved in proliferation and growth of tumour cells, with proved efficacy in prolonging survival in NSCLC patients that relapsed after chemotherapy, according to BR.21 study. Erlotinib is administered at 150 mg/day dose.

Methods. An observational study with erlotinib (Tarceva©) every other day (EOD) was conducted on unselected patients who experienced high grade toxicities with standard dosage of erlotinib 150 mg/day; these patients received erlotinib with personalized schedule of 150 mg every other day.

Results. From January 2007 to February 2011, 302 patients affected by non-small cell lung cancer (NSCLC), unselected for EGFR mutation, were treated with erlotinib 150 mg/day. 63.5% (192) were male and 36.5% (110) female with a median age of 62.1 (range 32-84); diagnosis was stage IV in more than 85% and histology was adenocarcinoma (ADK) in 62.2% (188), bronchiloalveolar carcinoma (BAC) in 10.3% (33), squamous carcinoma (SCC) in 21.1% (84) and not other specification (NOS) was 5.6% (17). Performance status was 0 in 17.8%, 1 in 44.3%, 2 in 28.8% and 3 in 8.9%. Forty-eight patients (27 ADK, 10 SCC, 8 BAC, 3 NOS) developed high grade (G3) toxicities during treatment with erlotinib 150 mg/day: skin rush (87.5%), diarrhoea (50%) and ocular discomforts (41.6%). In these patients, we continued treatment with erlotinib 150 mg EOD, with an improvement of toxicities and quality of life (QoL), and with a median progression-free survival (PFS) of 11.22 months (range 1-41).

Conclusion. This multicenter observational study showed that treatment with erlotinib 150 mg EOD reduces high-grade toxicities and does not affect survival. Long PFS survival with a customized schedule explains maintenance of drug steady state, with intermitting dose too, and with a higher compliance to the treatment by the patient.

D39 FREQUENT EPIGENETIC INACTIVATION OF *KEAP1* GENE IN NON-SMALL CELL LUNG CANCER

Muscarella L.A.[1], Parrella P.[1], D'Alessandro V.[2], la Torre A.[1], Barbano R.[1], Fontana A.[3], Tancredi A.[4], Guarnieri V.[5], Balsamo T.[1], Coco M.[1], Copetti M.[3], Pellegrini F.[3], De Bonis P.[5], Bisceglia M.[6], Scaramuzzi G.[4], Maiello E.[7], Valori V.M.[7], Merla G.[5], Vendemiale G.[2], Fazio V.M.[1,8]

[1]Laboratory of Oncology, [2]Internal Medicine Unit, [3]Unit of Biostatistics; [4]Thoracic Surgery Unit, [5]Medical Genetics Unit, [6]Department of Pathology, [7]Department of Oncohaematology, IRCCS "Casa Sollievo della Sofferenza" Hospital, San Giovanni Rotondo (FG), Italy; [8]Molecular Medicine and Biotechnology Laboratory, University Campus BioMedico, Rome, Italy

The KEAP1/NRF2 pathway is a master regulator of several redox-sensitive genes implicated in resistance of tumour cells against chemotherapeutic drugs. Recent data suggest that epigenetic mechanisms may play a pivotal role in the regulation of KEAP1 expression. We performed a comprehensive genetic and epigenetic analysis of the *KEAP1* gene in 47 non-small cell lung cancer tissues and 12 normal lung specimens. Promoter methylation analysis was performed using a quantitative methylation specific PCR assay in real time. Methylation at the *KEAP1* promoter region was detected in 22 out of the 47 NSCLCs (47%) and in none of the normal tissues analyzed. Somatic mutations were detected in 7 out of the 47 tumours (15%), and loss of heterozygosity (LOH) in 10 out of the 47 (21%) of the cases. Overall, we found at least one molecular alteration in 57% of the cases. Approximately one third of the tumours had two alterations and this feature was associated with higher risk of disease progression in univariate COX regression analysis (HR = 3.62; 95% CI 1.24-10.65, p = 0.02). This result was confirmed by Kaplan-Meier analysis which demonstrated an association between worst outcome and *KEAP1* double alterations (p = 0.01, Log-rank test). Our results further suggest that deregulation of the NRF2/KEAP1 system could play a pivotal role in the cancerogenesis of NSCLC. In addition, identifying patients with *KEAP1* genetic and epigenetic abnormalities may contribute to disease progression prediction and response to therapy in lung cancer patients.

D40 CLINICAL RELEVANCE OF HPV STATUS AND TREATMENT MODALITIES IN OROPHARYNGEAL CANCER (OC) PATIENTS (PTS)

Valduga F.[1], Caldara A.[1], Vanoni V.[2], Bragantini E.[3], Girlando S.[3], Vattemi E.[4], Magri E.[2], Bolner A.[2], Grandi C.[5], Tomio L.[2], Galligioni E.[1]

[1]Oncologia Medica, [2]Radioterapia, [3]Anatomia Patologica, [4]Otorinolaringoiatria, Ospedale S. Chiara, Trento; [4]Oncologia Medica, Ospedale S. Maurizio, Bolzano

Aim. To analyze the correlation between p16 status, radiotherapy technique and outcome for OC and to evaluate the toxicity of concomitant treatment.

Materials and methods. Between September 2005 and September 2008, 62 patients with OC (35 with stage IV, all M0) were treated at our department with primary radiotherapy ± chemotherapy or cetuximab. Seventeen pts (27.4%) received 3D-planned simplified conventional three field-RT (3D-S), 22 (35.5%) 3D advanced conformal (3D-A) and 23 (37.1%) intensity modulation radiation therapy (IMRT) with simultaneous integrated boost (SIB). In 30 pts (48.4%) RT was combined with concomitant systemic treatment (cisplatin 100 mg/m^2 q 21 in 23 pts, weekly cisplatin 30 mg/m^2 in 2 and cetuximab in 5). HPV status was analyzed by p16 immunohistochemistry (CINtec® Histology V-Kit) and molecular biology.

Results. Twenty-seven pts (43.5%) were p-16 positive, and 35 (56.5%) negative. Both groups of p16-positive and p16-negative pts had similar distribution of stage and treatment modalities. At a mean follow-up of 28 months (5-61) 3y-DFS for p16-positive and p16-negative pts was 76.2% and 58.4% respectively (p = 0.03) and correspondent 3y-OS was 68.2% and 44.1% (p = 0.002). In the p16-positive group, 3y-DFS was similar for the 3 RT modalities. In p16-negative pts, instead, 3y-DFS increased from 30% to 63% and to 87% with 3D-S, 3D-A and IMRT respectively (p = 0.05). Moreover IMRT was well tolerated also when was associated to concomitant systemic treatment (10 pts). Major remaining toxicities of the concomitant treatments consisted in G3 mucositis in 16 pts and G3 haematologic toxicity in 3. In pts treated with cetuximab we did not observe worse side ef-

fects than expected with RT alone, except for cutaneous toxicity (G1 in 2 pts, G2 in 1, G3 in 1).

Conclusions. It appears from our experience that HPV positive pts have a better prognosis, according to literature, and that IMRT with SIB seems to be more relevant for outcome in p16-negative pts and feasible also when associated with systemic treatment.

D41 OBSERVATIONAL STUDY WITH CARBOPLATIN, DOXORUBICIN, CYCLOPHOSPHAMIDE, VP16 AND VINCRISTIN (ACOCEV) AS A WEEKLY SEQUENTIAL SCHEDULE FOR POOR PERFORMANCE (PS) STATUS/ELDERLY SMALL CELL LUNG CANCER (SCLC) PATIENTS

Lucchini E., Frizziero M., Tondulli L., Parolin V., Cingarlini S., Gilioli E., Iannucci A., Molino A., Cetto G., Santo A.

GIVOP (Gruppo Interdisciplinare Veronese Oncologia Polmonare), Azienda Ospedaliera Universitaria Integrata, Verona

Introduction. The current treatment for a peculiar rapid-growth early metastatic disease such as SCLC is represented by chemotherapy with platinum plus VP-16, actually able to provide high response rate at first, while the early development of drug resistance is frequent. As a theoretical principle, an increase in disease control may be obtained by adopting a sequential dose-intense (such as weekly) regimen employing chemotherapeutics with both non-cross resistant mechanism of action and non-overlapping toxicities.

Methods. Elderly or poor PS pts affected by SCLC referring to the GIVOP were considered eligible for the current observational study. Treatment schedule consisted in the sequential administration of the ACOCEV regimen (doxorubicin 30 mg/m^2, cyclophosphamide 400 mg/m^2 on day 1 of every first week, vincristin 1.4 mg/m^2 on day 1 of every second and fourth week, carboplatin AUC 4 and VP16 60 mg/m^2 on day 1 of every third week, every 28 days for 3 to 4 cycles).

Results. From March 2005 to July 2010, 24 pts were consecutively enrolled. Activity and safety were evaluated in 18 pts who completed 2 courses of chemotherapy. Median age: 71.5 years (range 54-84); 11 (61%) and 4 pts had a PS-ECOG of 2 or 3, respectively. Fifteen patients (84%) presented with extensive disease (ED) and 6 patients (33.3%) were previously treated. An overall response rate of 72% (all partial responses) was achieved; 4 pts experienced disease progression (22%), 1 patient stable disease. Median time-to-progression was 5.5 months. 22% of pts experienced G3-4 neutropenia, without febrile episodes, and 5% of pts G3-4 thrombocytopenia. 22% of pts experienced G2 neurotocixities (paresthesia), with 2 and 3 pts reported alopecia and constipation, respectively.

Conclusions. The ACOCEV schedule seems feasible in the mixed population of elderly and poor-PS SCLC pts, by providing an extremely tolerable safety profile and a significant clinical benefit. A prospective investigation in a larger sample is mandatory.

D42 SEQUENTIAL CHEMOTHERAPY WITH CISPLATIN PLUS VINORELBINE FOLLOWED BY WEEKLY DOCETAXEL IN LOCALLY ADVANCED OR METASTATIC NON-SMALL CELL LUNG CANCER: PRELIMINARY RESULTS

Degli Esposti C., Melotti B., Sperandi F., Berselli A., Martoni A.

Medical Oncology Unit, S. Orsola-Malpighi Hospital, Bologna, Italy

Background. The use of platinum-based therapy prolonged survival in patients with NSCLC. A platinum-based doublet with a third-generation agent (vinorelbine, gemcitabine, paclitaxel, docetaxel) represents the standard first-line treatment for advanced NSCLC with good performance status. Traditional chemotherapy provides response rates of 20-40% and a median survival of 8-10 months. In an attempt to improve outcome, alternative schedules have been proposed, namely sequential, alternating, and maintenance/consolidation therapy. Sequential chemotherapy with a platinum-based doublet followed by a single agent is feasible in patients with a good PS. In our previous study, the planned sequential administration of GEM and VNR, in elderly patients with locally advanced or metastatic NSCLC, suggests that the TTP may be increased with the use of the 2 single agents.

Methods. On the grounds of these data we designed a phase II study on sequential strategy using weekly docetaxel (D) (35 mg/m^2 day 1 and 8 every 3 weeks) given after 3 courses of cisplatin (75 mg/m^2/iv day 1) and vinorelbine (25 mg/m^2/iv day 1 and 60 mg/m^2/os day 8) (PV) every 3 weeks as first-line treatment in patients with locally advanced, unresectable, or metastatic NSCLC. The treatment was continued until disease progression. All patients were restaged after every three courses by CT scan.

Results. Forty-one patients were enrolled from November 2008 to May 2011: 26 males and 15 females, median age 62 years (range 37-69), median PS 90% (range 60-100), 1 stage II-IA, 5 stage IIIB and 35 stage IV (11 pts with brain metastases); histology: 14 squamous and 28 non-squamous. At the moment all the patients are evaluable for toxicity and 36 for response. The overall best objective response was 17 (47%) partial response, 9 (25%) stable disease and 6 (17%) progressive disease. Toxicity was mild, the main side effect during PV was myelotoxicity, GI-II-IV neutropenia occurring in 10%. Median TTP was 23 weeks (range 1-91 weeks).

Conclusions. Sequential administration of cisplatin plus vinorelbine followed by weekly docetaxel in first-line treatment of advanced NSCLC was feasible, with high antitumour response and favorable toxicity profile. The study is ongoing.

D43 GEMCITABINE-CARBOPLATIN-PACLITAXEL (GEMCAP) AS INDUCTION CHEMOTHERAPY IN STAGE III NON-SMALL CELL LUNG CANCER (NSCLC)

Banna G.L.[1], Lipari H.[1], Buscarino C.[2], Seca A.[3], Ippolito M.[1], Novello G.[2], Cavallaro S.[2], Squatrito G.[4], Terminella A.[2], Saita S.[2]

[1]Division of Medical Oncology and Service of Nuclear Medicine, Cannizzaro Hospital, Catania, Italy; [2]Division of Medical Oncology, Unit of Functional Genomics and Division of Thoracic Surgery, Vittorio Emanuele University Hospital, Catania, Italy; [3]Unit of Radiotherapy, REM-Mediterranean Oncology Institute, Catania, Italy; [4]Service of Nuclear Medicine, Gravina Hospital, Caltagirone, Italy

Background. The combined use of gemcitabine (G), carboplatin (C) and paclitaxel (P) has proved to improve PFS and OS

of advanced stage IIIB and IV NSCLC in a phase II-III study, even if with considerable hematologic toxicity. In a previous dose finding study, we identified a safe GEMCAP regimen based on dose-limiting toxicities.

Methods. Patients aged 18-75 years, ECOG PS 0-1, with unresectable clinical stage IIIA or IIIB NSCLC suitable for definitive radiation treatment, were treated in a phase II study with C AUC 5 i.v., P 175 mg/m^2 i.v. on day 1, and G 800 mg/m^2 i.v. on days 1 and 8, every 3 weeks for 3 cycles. Patients with stage IIIA disease in response following GEMCAP were reassessed for surgery; those with unresectable stage IIIA and IIIB disease, were treated with radiotherapy. Primary endpoint was overall response rate (ORR). Secondary endpoints included: toxicity, progression-free survival (PFS), resection rate, and overall survival (OS).

Results. Of the 53 enrolled patients, 42 were males, 11 females, 29 (55%) patients were in stage IIIA, 24 (45%) in stage IIIB NSCLC, 27 (51%) had adenocarcinoma, 19 (36%) squamous cell carcinoma, 47 (89%) PS 0. Forty partial responses and one complete response were observed, for an ORR of 80%. G3-4 and G2 toxicities, occurring in ≥5% of patients, included: neutropenia (19-8%), hypertransaminemia (11-2%), diarrhoea (6-0%), G3-4 toxicities; neutropenia (34%), asthenia (25%), diarrhoea (15%), peripheral neuropathy (13%), osteomyalgia (11%), hypertransaminemia (6%), nausea/vomiting (9%), G2 toxicity. With a median follow-up of 20 months (range 6-77), PFS was 10.5 months (95% CI, 9.9-11.4); OS was 21.1 months (95% CI, 19.6-22.9). Thirteen patients were operated, for a resection rate of 44%.

Conclusions. The GEMCAP regimen, at the employed dose, demonstrated a considerable response and resection rate, with acceptable toxicity, as induction chemotherapy for clinical stage III NSCLC. PFS and OS compared favourably with those expected for clinical stage III disease.

D44 THE ROLE OF PEMETREXED IN THE TREATMENT OF MALIGNANT PLEURAL MESOTHELIOMA. A RETROSPECTIVE COMPARISON AMONG PEMETREXED AND NON-PEMETREXED BASED PALLIATIVE CHEMOTHERAPIES

Pazè E.[1], Sambuco A.[1], Mirabelli D.[2], Ruffini E.[3], Gangemi M.[2], Bruna M.C.[3], Ciuffreda L.[1]

[1]S.C. Oncologia 1, A.O.U. S. Giovanni Battista di Torino; [2]SCDU Epidemiologia dei Tumori, Università di Torino and CPO Piemonte; [3]SCDU Chirurgia Toracica, A.O.U. S. Giovanni Battista di Torino

Introduction. Treatment of malignant pleural mesothelioma (MM) remains disappointing despite use of combined therapies. Pemetrexed is an antifolic drug which has proved to be active on MM and has been approved as first-line chemotherapy associated with cisplatin. We compared the MM patients treated at our Institution with and without pemetrexed-based chemotherapy in order to evaluate the contribution of this drug.

Materials and methods. We retrieved the data concerning all MM patients treated at our Oncological Unit in the period 2000-2010. We identified 81 MM patients who had been treated with first-line palliative chemotherapy. None of them had received radical surgery. Twenty-six patients had received non-pemetrexed first-line chemotherapy and 55 had received a pemetrexed-based chemotherapy. Three among non-pemetrexed patients and 5 among pemetrexed patients had undergone partial pleurectomy. One non-pemetrexed patient and 3 pemetrexed patients presented with peritoneal disease at diagnosis. As pemetrexed can be a well tolerated drug it has been often used also as single agent therapy. We therefore evaluated also survival among those patients who received a platinum-based chemotherapy, which were 19 among the non-pemetrexed patients and 42 among the pemetrexed patients.

Results. The median overall survival (MOS) among the 26 non-pemetrexed patients was 14 months (range 1-66 months); among pemetrexed patients it was 12 months (2-49). Among patients who received a platinum-based chemotherapy MOS was 15 months (3-27) for the non-pemetrexed group and 14 months (2-49) for the pemetrexed one.

Discussion. In our single-institution experience, no differences in MOS were detected after the introduction of pemetrexed in MM patients treated with palliative chemotherapy. Further prospective studies are needed to confirm our data.

	Non-pemetrexed treated patients	Pemetrexed treated patients	All patients
Non-platinum treated patients			19 patients MOS 10 mo (2-66)
Platinum treated patients	20 patients MOS 14.5 mo (1-27)	42 patients MOS 14 mo (2-49)	62 patients MOS 14 (1-49)
All patients	26 patients MOS 14 mo (1-66)	55 patients MOS 12 mo (2-49)	81 patients MOS 12 mo (1-66)

D45 EGFR AND K-RAS STATUS AND CLINICAL OUTCOMES IN PATIENTS WITH ADVANCED NSCLC TREATED WITH ERLOTINIB: OUR EXPERIENCE

Di Cocco B., Salesi N., Colonna M., Veltri E.S.A.

U.O.C. Oncologia Sud ASL Latina, Ospedale "Di Liegro" Gaeta (LT)

Background. The purpose of this analysis was to investigate in patients with advanced NSCLC pre-treated, the response to erlotinib, EGFR tyrosine kinase inhibitor (TKI), and EGFR and K-Ras mutations.

Methods. Sixty-three patients with stage IIIB or IV non-small cell lung cancer, with performance status from 0 to 2, previously treated with 1-2 chemotherapy regimens received erlotinib (150 mg oral daily). We also analyzed 63 tumour samples for EGFR/K-Ras mutations by fluorescence *in situ* hybridization (FISH; EGFR gene copy number), and DNA sequencing (EGFR, KRAS gene mutations). Coprimary endpoints were overall response rate (ORR) and clinical benefit (CB) in according to EGFR/K-Ras status. Secondary endpoints were progression-free survival (PFS) and safety.

Results. Among 63 patients, 4 had a partial response (ORR 6.35%),with median duration of the response of 12 months (mo), 16 had a stable disease (SD 25.4%) with CB of 31.75%; PSF was 2.2 mo. Nine patients (14.2%) had EGFR mutations, 7 (11.1%) had K-Ras mutations, 18 (28.5%) showed a high level of EGFR gene copy (FISH positive). Two of 9 patients with EGFR muta-

tion had a RP, 4 had a SD (66.6% CB) compared with 2 RP and 12 SD (CB 25.9%) in the group with wild type EGFR (54 pts). PFS of 9 pts with EGFR mutation was 8.5 mo. 3/18 pts EGFR FISH positive had RP. None of the 4 patients with a K-Ras mutation (4.76%) had a tumour response. Only 3% of patients discontinued erlotinib because of toxic effects.

Conclusions. According to the literature our data show that the presence of EGFR mutations seems to correlate with response to erlotinib with improved clinical benefits and PSF.

D46 SINGLE-AGENT ORAL NAVELBINE IN VERY ELDERLY NSCLC PATIENTS

Filipazzi V., Cattaneo M.T., Isabella L., Gambaro A., Tosca N., Ferrario S., Fasola C., De Troia B., Farè E., Somma L., Mauceri A., Damiani E., Curcio R.°, Vimercati S.°, Piazza E.

Oncology Department, °Pharmacia Department, "L. Sacco" Hospital, Milan.Italy

Background. Elderly patients with advanced non-small cell lung cancer (NSCLC) are a special population requiring particular attention. Single-agent chemotherapy is considered the standard treatment[1] and oral vinorelbine could be an attractive option to this kind of patients.

Patients and methods. A total of 26 patients with stage IV NSCLC, (ECOG) PS 1-2 with good functional status were recruited. Oral vinorelbine was administered at the dose of 60 mg/m^2 on days 1-8 every 3 weeks. Primary endpoints were safety, response rate and PFS.

Results. The characteristics of patients were 23 M +3 F, median age 80 years (range 75-86), 11 were squamous cell carcinoma, 10 were adenocarcinoma and 5 NSCLN (NOS).

Oral chemotherapy was performed in all patients with median of 3 courses (range 1-6).

We record only 1 partial response; 14 pts experienced stable disease lasting more than 12 weeks and 11 pts showed disease progression for an overall clinical benefit of 15/26 (57%).

Median time to progression was 3 months (range 2-8) and median overall survival was 10 months (range 3-24). Treatment was well tolerated. Of 89 cycles performed, we did not observe any grade 3/4 toxicity with the exception of a single not-febrile G3 neutropenia. Regardless of tolerability the main toxic effects observed were nausea in 62% and vomiting in 20% of patients, anemia in 15%, fatigue in 32% and leukopenia in 30%.

Conclusion. Single-agent oral vinorelbine is extremely safe in elderly patients with advanced NSCLC and may represent a valid option in this very special population.

References

1. Gridelli C: The ELVIS trial: a phase III study of single-agent vinorelbine as first-line treatment in elderly patients with non-small cell lung cancer. Elderly Lung Cancer Vinorelbine Italian Study. Oncologist, 6 (1): 4-7, 2001.

D47 ZOLEDRONIC ACID ROLE IN SREs PREVENTION: AN ADVANTAGE FOR ALL PATIENTS WITH ADVANCED NSCLC AND BONE METASTASES?

Del Signore E.§, Gori B.§, Intagliata S.*, Ricciardi S.§, Fulvi A.§, Belli R.§, Di Salvia M.§, Migliorino M.R.§, de Marinis F.§

*§Oncological Pulmonary 1st Unit, San Camillo-Forlanini Hospitals, Rome, Italy; *Medical Oncology Department, University Campus Bio-Medico, Rome, Italy*

Introduction. The effectiveness of bisphosphonates (BPs) in preventing, reducing the incidence, and delaying the onset of skeletal-related events (SREs) in patients (pts) with bone metastases (BM) was demonstrated in wide spectrum of solid tumours, including lung cancer. The purpose of this study is to investigate the impact of zoledronic acid (ZA) administration in prevent SREs in pts with advanced non-small cell lung cancer (A-NSCLC).

Methods. We observed retrospectively 148 pts with NSCLC and BM diagnosed (2007-2010) at the same time of the primary tumour or later during the treatment. The effectiveness of treatment with ZA was valued in terms of time at the diagnosis of bone metastasis and time at first or second SREs during the treatment. Furthermore we valued the effectiveness of treatment to relieve pain (Visual Analogic Scale) and improve quality of life (EORTC-QoL Scale). Overall survival also was considered. Bone assessment should be based on CT body scan, positron emission tomography (if available) or bone scan.

Results. At the moment we analyzed 58/148 pts. Median age was 61 years. In 43% BM was observed at the time of diagnosis of primary disease, in 57% during the chemotherapy. After diagnosis of BM, pts were treated with ZA at the standard dose of 4 mg every 28 days. Bone pain was observed in 80% of pts and in 60% it decreased during the treatment with ZA associated with improved QoL. The first SRE occurred at the time of the diagnosis in 26 pts (45%). During the treatment with ZA, 13 pts (22%) experienced the first SRE. Among these, 4 pts (30%) had BM at the diagnosis of disease and experienced the first SRE after 2 months of treatment; 9 pts (70%) developed BM during antineoplastic treatment and experienced the first SRE after 9 months of treatment with ZA. Nineteen pts (33%) never experienced SREs. In no pts adverse effects occurred.

Conclusions. This retrospective analysis about role of zoledronic acid to prevent SREs in NSCLC pts with BM is ongoing but it's emerging a prognostic difference between BM diagnosed at the time of primary disease and those diagnosed during antineoplastic treatment. Final data will be presented at the AIOM congress.

D48 SURGERY + RADIOTHERAPY VS EXCLUSIVE CHEMO-RADIATION THERAPY REGIMENS IN ORAL AND OROPHARYNGEAL CANCER: LONG TERM TOXICITY EVALUATION

Garzaro M.[1], Airoldi M.[2], Raimondo L.[1], Riva G.[1], Pecorari G.[1], Giordano C.[1]

[1]1st ENT Division, Physiopathology Department, University of Turin, Turin, Italy; [2]2nd Medical Oncology Division, San Giovanni Battista Hospital, Turin, Italy

Purpose. Treatment of head and neck tumours negatively affects speech, swallowing, and quality of life (QoL). Our aim was the evaluation of long term toxicity comparing surgery + radio-

therapy (S+RT) and exclusive chemo-radiation therapy (CH-RT) regimens.

Patients and methods. Seventy-two patients, homogeneous for demographic and TNM characteristics were affected by a tumour of oral cavity and oropharynx; 36 underwent S+RT and 36 received exclusive CH-RT. Late effects of treatment assessment included: Radiation Therapy Oncology Group (RTOG)-European Organisation for Research and Treatment of Cancer (EORTC) late radiation morbidity scoring system, DISCHE morbidity recording scheme.

Results. According to AJCC TNM 7th edition, in S+RT group, 58% of pts was T1/T2, 42% T3/T4, 39% N0/N1, 61% N2/N3, 22% stage I/II, 78% stage III/IV, 64% G1-G2 and 36% G3. In CH-RT group 55% of pts was T1/T2, 45% T3/T4, 41% N0/N1, 59% N2/N3, 19% stage I/II, 81% stage III/IV, 62% G1-G2 and 38% G3. After median follow-up of 63 months, moderate-severe DISCHE score in S+RT vs CT+RT was: skin toxicity (86% vs 81%), subcutaneous fibrosis (97% vs 75%), taste impairment (64% vs 89%), salivary function (59% vs 79%). Long-term dysphagia: some discomfort (22% vs 39%), soft diet required (42% vs 28%), fluids only and naso-gastric tube feeding (11% vs 4%).

Conclusion. A different pattern of long-term toxicity was observed in S + RT vs CT + RT. Anxiety rate is lower, depression is present in half of patients and is statistically related with dysphagia.

D49 THE CLINICAL SIGNIFICANCE OF NEURON-SPECIFIC ENOLASE (NSE) BLOOD LEVELS IN NON-SMALL CELL LUNG CANCER (NSCLC): PRELIMINARY CONSIDERATIONS

Mancin M., Cortinovis D., Cicchiello F., Canova S., Cazzaniga M., Crippa A., Lissoni P., Bidoli P.

Division of Medical Oncology, San Gerardo Hospital, Monza, Italy

Background. NSE is commonly considered as a specific marker for small cell lung cancer (SCLC). Preliminary studies would suggest a possible increased production of NSE also in NSCLC patients. To further define the significance of NSE in NSCLC, we have evaluated its serum levels in a group of patients affected by advanced NSCLC.

Patients and methods. The study included consecutive stage IV NSCLC patients, who were hospitalized at the Division of Medical Oncology of San Gerardo hospital. NSE levels were considered to be abnormally high when they were greater than 3 SD with respect to the normal values, corresponding to concentrations higher than 20 ng/mL.

Results. From 06/2010 to 03/2011, 45 serum samples were analyzed. The population's main clinical characteristics were: M/F 28/17; median age 64 years (36-81); histotype: adenocarcinoma 34, squamous cell carcinonoma 8, large cell carcinoma 3; 18 patients untreated, whereas the other 27 patients received at least one chemotherapeutic line. NSE increased levels were seen in 20/45 (44%) patients, without significant differences between patients with adenocarcinoma and those with other histotypes (14/35 vs 6/10). No significant difference in NSE mean (± SE) levels between adenocarcinoma and squamous cell cancer patients (23.8 ± 3.2 vs 23.6 ± 3.5 ng/mL). NSE mean values were higher in patients with visceral metastases (n = 34) than in those with bone and/or soft tissue lesions (n = 11) (25.9 ± 3.6 vs 21.3 ± 2.7 n/mL), without statistically significant differences.

Conclusions. These preliminary results show that NSE may be increased also in patients with NSCLC without differences among sub-histotypes. Several experimental studies have already demonstrated the existence of a neuroendocrine fraction in most lung neoplasms, irrespectively of their histotype, which could explain the enhanced NSE production. Further studies, by correlating NSE variations to the clinical response to chemotherapy, will be required to establish the prognostic significance of NSE in NSCLC.

D50 LONG-TERM QUALITY OF LIFE, PHYSICAL AND PSYCHOLOGICAL FUNCTIONING IN RELAPSED HEAD AND NECK CANCER PATIENTS

Airoldi M.[1], Garzaro M.[2], Raimondo L.[2], Riva G.[2], Pecorari G.[2], Giordano C.[2]

[1]2nd Medical Oncology Division, San Giovanni Battista Hospital, Turin, Italy; [2]1st ENT Division, Physiopathology Department, University of Turin, Turin, Italy

Purpose. Primary head and neck squamous cell carcinomas (HNSCC) and their recurrences can heavily affect patient's quality of life (QoL). Aim of our study was the evaluation of the impact of treatment on QoL, physical and psychological functioning of patients affected by recurrent HNSCC.

Patients and methods. The sample was composed by 34 patients affected by recurrent HNSCC. Primary tumour treatment was as follows: exclusive RT (radiotherapy) 18%, S+RT 55%, RT + chemotherapy (CT) 27%. In order to evaluate the late effects of RT we used the RTOG-EORTC late radiation morbidity score plus the DISCHE morbidity recording scheme.

Psycho-oncological assessment included: HADS, MADRS, MINI MAC, EORTC QoL HN 35.

Results. Among this population, 55% of pts relapsed on T, 15% on N, 21% on T+N and 9% on M. Recurrences were treated with S+CT 6%, RT+CT 21% and CT alone 73%. The late toxicity evaluation demonstrates that skin alterations, salivary glands impairment, subcutaneous fibrosis and mucous membrane alterations are the most relevant and severe damages.

After a median follow-up of 60 ± 26 months, analysing RTOG-EORTC scale, high scores of skin and mucous membrane alterations are related ($p < 0.05$) with higher levels of anxiety and depression, negative coping styles (reduction of fighting spirit, anxiety and depression) are increased by salivary and mucous membrane dysfunctions ($p < 0.05$), moreover lower levels of QoL, in particular physical and social functioning, are correlated with higher levels of mucous membrane damages ($p < 0.05$); all the mentioned above symptoms increase negative thoughts ($p < 0.05$). DISCHE findings are superimpose able.

Conclusion. Treatment of relapsed HNSCC added to surgery and or RT and or CHT on the primary tumour could result in a heavy addictive effect on mucous membrane, skin, subcutaneous tissues and salivary glands referred symptoms. Negative coping styles and thoughts, increased anxiety and depression and lower levels of QoL are strongly associated to high scores of such symptoms.

D51 ERLOTINIB IN CHEMO-REFRACTORY NON-SMALL CELL LUNG CANCER (NSCLC): CLINICOPATHOLOGIC FEATURES BEYOND EGFR MUTATIONS

Inno A.[1], De Luigi N.[1], Capodimonti S.[2], Martini M.[2], Plastino F.[1], Marsico V.A.[1], Strippoli A.[1], Larocca L.M.[2], Pozzo C.[1], Barone C.[1]

[1]Division of Medical Oncology, [2]Institute of Pathology, Università Cattolica del Sacro Cuore, Roma

Background. EGFR mutations predict efficacy of first-line gefitinib in metastatic NSCLC pts, whereas is not clear whether they are also predictive for erlotinib in second-line and maintenance setting. Prospective clinical trials specifically addressing this issue are ongoing.

Methods. From 2008 to 2010, 80 NSCLC chemo-refractory pts were treated at our institution with erlotinib 150 mg/day. EGFR mutational analysis was performed on available tumour samples.

Results. Median age was 65, males and females were respectively 55.1% and 44.9%. 34.6% of pts was never-smoker, 75% had 0-1 ECOG PS and 70.5% received erlotinib as second-line, whereas the other pts received erlotinib in third- or even fourth-line. Tissue sample for EGFR analysis was available from 42 pts. Four (9.5%) EGFR activating mutations were found among 42 tissue samples, and all mutated tumours were adenocarcinoma. Overall response rate (RR) was 20.9% and median PFS was 4 months. A trend of better response and longer PFS was observed for mutated pts when compared to wild-type ones (RR 50% vs 10.5%, p = .091; PFS 9 vs 3 months, HR 0.55, p = 0.18). Outcome was significantly influenced by gender (females and males, respectively: RR 50% and 10.5%, p = .002; HR for progression 0.50, p = .001) and by smoking history (never-smokers and current or former smoker, respectively: RR 37% and 11.8%, p = .016; HR for progression 0.45, p <.001). HR for progression also significantly favoured pts with adenocarcinoma (HR 0.59, p = .049) and those with PS of 0-1 (HR 0.49, p = .004).

Conclusions. A clinical selection based upon gender, smoking history and histology may be useful to select pts who potentially will get a survival benefit from erlotinib. The retrospective nature and small sample size of our study do not allow to draw definitive conclusions about the role of EGFR mutations. However, since some EGFR wild-type pts achieved a possible benefit from erlotinib, other predictive biomarkers should be investigated.

D52 EFFECTIVENESS OF ERLOTINIB IN LUNG CANCER PATIENTS

Castorino N.[1], Sichetti D.A.P.[1], Fanizza C.[1], Corrado D.[1], Belfiglio M.[1], Romero M.[1], Orsini A.[2], Melena S.[3] on behalf of PROMOFIA Oncologic Working Group*

[1]Department of Clinical Pharmacology and Epidemiology, Consorzio Mario Negri Sud, Santa Maria Imbaro (Chieti); [2]Pharmacovigilance service, Abruzzo Region, Teramo; [3]Pharmaceutical Care Service, Direction of Health Policy, Abruzzo Region, Pescara

*PROMOFIA Oncologic Working Group: Antonelli D., Caliendo G., Cioffi P., Corridoni S., D'Ercole F., De Plato F., Margiotta F., Petragnani G.

Background. Erlotinib, an EGFR tyrosine-kinase inhibitor, is a new oncological drug approved for maintenance treatment of patients with stage IIIB/IV non-small cell lung cancer (NSCLC).

As part of PROMOFIA study, this work aimed to evaluate overall survival (OS) and progression-free survival (PFS) of patients receiving erlotinib for lung cancer in clinical practice.

Methods. An observational prospective study, with a follow-up of 12 months, has been performed in Abruzzo by 2008 to identify all patients receiving new oncological drug for any indication.

To identify prognostic factors associated with OS and PFS, a multiple Cox proportional hazard model was used.

Results. Overall 242 patients with stage III-IV lung cancer treated with erlotinib were included: median age 70 years (range 30-87); 23.1% women; 75.2% with 0-1 ECOG performance status (PS); 87.2% had metastases; 90.1% with NSCLC. Almost all patients (97.5%) received at least one prior chemotherapy regimen.

One hundred and twenty-five deaths (51.6%) occurred; median OS was 8.6 months. In Cox analysis, men (adjusted HR = 2.00; 95% CI 1.23-3.25; p = 0.005) and patients with 2-4 ECOG-PS (adjusted HR = 2.53; 95% CI 1.73-3.68; p <0.001) were associated with a higher mortality.

One hundred and ninety-three patients had progression of disease (79.7%); median PFS was 3.8 months. In Cox model, men (adjusted HR = 1.50; 95% CI 1.05-2.15; p = 0.02) and patients with 2-4 ECOG-PS (adjusted HR = 1.74; 95% CI 1.26-2.40; p <0.001) were associated with a higher incidence of progression or death, as well as younger patients (≤60 yrs) (adjusted HR = 1.68; 95% CI 1.11-2.53; p = 0.01) compared to the elderly over 75 years.

The 5.9% of patients discontinued erlotinib because of toxicity.

Conclusions. The study is ongoing. This interim analysis shows that in clinical practice survival profile of patients receiving erlotinib for lung cancer is longer than pivotal study BR.21 (OS: 8.6 vs 6.7 months; PFS: 3.8 vs 2.2 months). This could be due to differently epidemiological-clinical characteristics (in our study patients were older, more men, with a better ECOG-PS).

These results, even if preliminary, show the actual effectiveness of erlotinib in NSCLC.

D53 ACTIVITY OF ERLOTINIB IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) AND EARLY PROGRESSION DURING FIRST-LINE PLATINUM-BASED CHEMOTHERAPY

Biondani P., Pietrantonio F., Vitali M., Buzzoni R., Di Bartolomeo M., Formisano B., Testa I., Platania M., Zilembo N.

Medical Oncology Unit 2, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy

Background. Patients with advanced NSCLC progressing during first-line platinum-based chemotherapy display an extremely poor prognosis: the shorter is time to second-line chemotherapy, the worst is survival (Weiss, 2006). The effect of first-line chemotherapy outcome on second-line anti-EGFR treatment was not clearly established. Progressive disease on prior treatments was predictive of early progression and death in a separate analysis of BR.21 trial of erlotinib (E) versus placebo as second/third-line treatment of NSCLC (Florescu, 2008).

Materials and methods. The aim of this retrospective analysis was to assess the efficacy of E in advanced NSCLC pts with early progression during first-line platinum based chemotherapy. We reviewed 34 consecutive patients treated with second/third-line E at a single Institution from October 2006 to April 2011. Eligibility criteria: advanced NSCLC, early progression demonstrated at 6 or 12 weeks from the start of first-line platinum-based chemotherapy, ≤2 prior chemotherapy regimens.

Results. Patients characteristics were as follows: M/F, 20/14, current or former smokers/light or never smokers, 26/8, adenocarcinoma/bronchioloalveolar/squamous-cell/other, 23/4/5/2, ECOG PS 0-1/2, 26/8, E second/third-line, 17/17. In the overall population activity of E was modest: response rate 4/34, 12%; median response duration, 8 months (range 6-48); progressive disease 30/34, 88%; median time-to-progression, 7 weeks; median overall survival, 3 months; treatment start within last 30 days of life, 24%. Characteristics of pts responding to E: 4/4 non-smokers, 3/4 females, 3/4 EGFR-mutated, 2/4 bronchioloalveolar histology. Additional chemotherapy beyond first-line (mainly docetaxel or pemetrexed) was administered to 20 pts (59%): only 3 stable disease were obtained, with a median time-to-progression of 9 weeks.

Conclusions. E shows limited activity in unselected NSCLC patients with early progression during first-line platinum-based chemotherapy. Nevertheless, clinically and/or biomolecularly selected patients can obtain significant benefit from EGFR-targeted salvage treatment.

D54 CONCURRENT INTRA-ARTERIAL CARBOPLATIN ADMINISTRATION AND RADIATION THERAPY FOR THE TREATMENT OF ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMA: LONG TERM RESULTS

Corbella F., Bertino G., Porta C., Zappoli F., Morbini P., Mura F., Occhini A., Colombo S., Paglino C., Di Liberto R., Quaretti P., Pedrazzoli P., Benazzo M.

Gruppo multidisciplinare neoplasie del distretto cervico-cefalico, Fondazione IRCCS, Policlinico S. Matteo, Pavia

Background and aim. Previous reports suggest that excellent locoregional control rates are achievable in patients with advanced head and neck (H&N) cancer by combining intra-arterial delivery of platinum salt and concurrent radiotherapy (RADPLAT). The aim of the present study was to evaluate clinical outcome and safety of a modified RADPLAT protocol (Bertino G et al, BMC Cancer, 9: 313, 2009) using carboplatin instead of high dose cisplatin.

Patients and methods. Sixty-five patients (52 male; median age 52 years, range 38-74) with advanced H&N squamous cell carcinoma. Disease site was oropharynx in 34, oral cavity in 27, hypopharynx in 3 and larynx in 1. Treatment protocol consisted of selective intra-arterial administration of carboplatin (350 mg/m^2 every 2 weeks for 4 cycles), with concurrent three-dimensional conformal radiation therapy (RT). Radiotherapy was administered in fractions of 1.8/2 Gy for 5 days a week: PTV I (T) received 66-74 Gy, PTV II (N+) received 56-66 Gy, PTV III (N0) received 50-60 Gy.

Results. Two major (1 myocardial infarction, 1 partial tongue necrosis) and 4 minor (cutaneous rush, oedema) acute complications were observed. Fifty-six of the 65 patients (80%) completed the protocol, 9 having received only 3 courses of CT due to haematological toxicity while completing RT. No patients required tube feeding. Local control was achieved in 64 patients. With a median follow-up of 40 months (range 12-80), 36 patients (50%) are alive and disease-free. Twenty-nine patients have died of disease progression or other causes not related to the tumour. Distant recurrence occurred in 9 patients.

Conclusion. Concurrent chemoradiotherapy with a intra-arterial carboplatin is feasible for patients with advanced H&N cancer and provides long term control of local disease.

D55 PILOT SINGLE INSTITUTIONAL EXPERIENCE ON TOLERANCE AND CLINICAL EFFICACY OF METRONOMIC CHEMOTHERAPY WITH ORAL VINORELBINE IN UNFIT PATIENTS WITH ADVANCED OR METASTATIC NON-SMALL CELL LUNG CANCER (NCSLC)

Del Conte A., Saracchini S., Santeufemia D.A., Lo Re G., Tumolo S.

U.O. Oncologia Medica, Azienda Ospedaliera "S. Maria degli Angeli", Pordenone

Background. Metronomic chemotherapy (MC) is a new dosing strategy of administration subtoxic doses of chemotherapy over protracted periods of time with the aim to target tumour angiogenesis. Same papers demonstrate that oral vinorelbine (o-VNR) given as MC has a good tolerability and efficacy in breast cancer. In NSCLC the MC is lacking.

Methods. This is a monoinstitutional pivotal experience in patients with stage IIIB-IV NSCLC, uneligible for platinum-based chemotherapy due to one or more of these reasons: age >80 yrs, performance status (PS) >2 or severe comorbidity. Patients were treated with o-VNR increasing doses. The starting dose was 40 mg three times a week (tw) on Monday, Wednesday and Friday without week rest. Dose was escalated by 10 mg increments, in the absence of severe toxicity.

Results. Twenty-one patients were included in the study and were treated in three dose levels. The median age was 75 years (range 59-86). The treatment lines were: 12 1st, 3 2nd, 5 3rd and 1 4th. Fifteen patients were treated at 40 mg tw. Three out of 15 pts increased the dose to 50 mg and one to 60 mg tw. Other six patients started with 50 mg tw.

Toxicities	G3	G4
Leuconeutropenia	2/21 (9.5%)	none
Diarrhea	3/21 (14%)	none
Asthenia	4/21 (19%)	none
Peripheral neuropathy	none	none

Patients evaluable for response (PE) were 17 (4 still on treatment). The number of PE with PS 1/2/3 were respectively 5/5/7. The disease control rate was 29% (5 pts): 1 partial response and 4 stable disease (1 of these persisted for 10.8 months). The median PFS and OS were respectively 2.6 (range 0.9-10.8) and 4.5 months (range 2.0-15.5). The mOS differed significantly according to the patient's PS: respectively 11.1/4.2/4.5 months for PS 1/2/3. Three out of 5 patients in PS1 are still alive.

Conclusions. Metronomic o-VNR can be safely administered to elderly and very unfit patients with NSCLC and reveal a modest activity in this population. The prolonged mOS in PS1 patients suggests that this strategy could be particularly useful in elderly patients (>75 yrs) with good PS. Of course, the data presented should be confirmed on a larger sample of patients.

D56 ADVANCED NSCLC PATIENTS AGED OVER 80 YEARS: TO TREAT OR NOT TO TREAT? THAT IS THE QUESTION!

Platania M., Agustoni F., Vitali M., Gelsomino F., Martinetti A., Zilembo N., Pietrantonio F., Formisano B., Buzzoni R.

Medical Oncology 2, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Background. The increasing prevalence in the population of elderly and very elderly persons generates important therapeutic needs that require optimal characterization of safety and efficacy of treatment approaches. Especially the very elderly may differ from younger patients in their response to drugs for a variety of reasons including a greater likelihood of concomitant illnesses and therapies. In elderly NSCLC pts, with adequate PS, platinum-based chemotherapy has been shown to improve both overall survival and quality of life. However, the treatment approach to this particular subset of patients is controversial and limited data exist since the very elderly population is under-represented in controlled clinical trials.

Patients and methods. We retrospectively reviewed the medical records of 22 pts aged ≥80 with diagnosis of NSCLC admitted between 2008 and 2010 at Istituto Nazionale Tumori of Milan. Data recorded included demographics, history of tobacco use, histology, PS, sites of metastases and treatment modalities. Comorbidities were evaluated using the Charlson comorbidity index (CCI). Adverse events were graded using CTCAE (v4.02) and tumour responses in accordance with RECIST criteria (v1.0).

Results. Patients characteristics: 13M/9F; median age 82 years (80-85); ECOG PS was 0-1 in 18 pts (80%) while CCI was ≥2 in 60% of cases. At diagnosis 19 (86%) pts were metastatic and 3 locally advanced; tumour histology: adenocarcinomas (14), squamous (5) and NOS (3). Fifteen pts received systemic therapy, 2 biological treatment and 5 were selected for BSC. The overall response rate was 18%, the median time-to-progression was 162 days and the median survival time (MST) was 249 days. Grade 3-4 hematological and non-hematological toxicity was 6% and 11%, respectively. The MST for pts who underwent BSC was 112 days.

Conclusion. If compared with historical controls, our data suggest that octogenarians with advanced NSCLC seem to get the same benefits than younger from medical treatment. However, an adequate characterization of the safety profile in the geriatric population is necessary and should include sufficient data from prospective studies.

D57 PEMETREXED (PEM) PLUS PLATINUM-BASED REGIMEN AS FIRST-LINE TREATMENT IN UNSELECTED PATIENTS AFFECTED WITH NON-SQUAMOUS NON-SMALL CELL LUNG CANCER (NSCLC): A RETROSPECTIVE MULTICENTER ANALYSIS

Ruggeri E.M.[1], Longo F.[2], Mansueto G.[3], Narducci F.[3], Sperduti I.[4], Martelli O.[5], Angelini F.[6], Pavese I.[7], Fabbri M.A.[1], Moscetti L.[1]

[1]UOC Oncologia, Ospedale Belcolle, AUSL, Viterbo; [2]UOC Oncologia A, Policlinico Umberto I, Rome; [3]Medical Oncology Unit, ASL Frosinone, Frosinone; [4]Biostatistics, Regina Elena National Cancer Institute, Rome; [5]UOC Oncologia, Ospedale Azienda Ospedaliera S. Giovanni-Addolorata, Rome; [6]UOC Oncologia, Ospedale Regina Apostolorum, Albano Laziale, Rome; [7]UOC Oncologia, Ospedale San Pietro Fatebenefratelli, Rome

Background. This multicenter analysis was performed to evaluate the outcomes in an unselected population affected with NSCLC treated with PEM plus platinum-based regimen.

Methods. 123 pts treated with PEM + platinum-based regimen were retrieved. Median age: 63 years; M/F: 67%/33%; ECOG PS 0-1: 94%; weight loss >5%: 21%; current smoker: 31%; stage IV: 81%; site of metastasis ≥1: 79%; brain metastasis: 14% of pts.

Results. 123 pts were analyzed. PEM + cisplatin have been administered to 81% of pts, and PEM + carboplatin to 19%. PEM maintenance was given to 21% of pts. The disease control rate achieved was 65% (PR 36%, SD 29%). The 1-yr OS and the 1-yr PFS observed were 51.4% and 17.4% respectively. At a median-FU of 6.7 months (range 1-22), the mOS was 13 months (95% CI: 9-16) and the mPFS: 6 months (95% CI: 5-8). No differences were seen in PFS and OS according to the response (PR or SD), type of regimen, smoking status and maintenance treatment versus not. A significant difference in 1-yr OS (63% vs 21%, p <0.0001) and in 1yr-PFS (28.5 vs 6%, p = 0.007) was observed for weight loss <5% vs >5%. In the Cox multivariate analysis a statistically significant difference was observed for: sex (M vs F, HR 2.1, 95% CI 1.17-3.8, p = 0.01); PS (0 vs ≥1, HR 2.12, 95% CI 1.24-3.64, p = 0.006); sites of disease (1 vs ≥2, HR 2.38, 95% CI 1.07-5.29, p = .03); response (PR vs no response, HR 3.48, 95% CI 1.98-6.14, p <0.0001). A trend in improvement for PEM maintenance was seen in the 1-yr OS (72% vs 55%, p = 0.07) whereas not for 1yr-PFS (29% vs 22%, p = ns). No difference in the outcome was seen for patients achieving a PR or SD and receiving PEM maintenance or in pts with brain metastases.

Conclusion. This retrospective analysis compares favourably with the data achieved in the registration study and confirms the activity of the PEM + platinum-based regimen also outside clinical studies.

D58 SHOULD THE USE OF EGFR TYROSINE KINASE INHIBITORS BE LIMITED TO NSCLC PATIENTS WITH EGFR MUTATIONS?

Sperandi F.[1], Melotti B.[1], Berselli A.A.[1], Fiorentino M.[2], Degli Esposti C.[1], Altimari A.[2], Gruppioni E.[2], Martoni A.A.[1]

[1]Medical Oncology Unit, [2]Pathology Unit, S. Orsola-Malpighi Hospital, Bologna

Background. Somatic mutations in the epidermal growth factor receptor (EGFR) most often display adenocarcinoma histology and correlate with increased response and prolonged survival in patients (pts) with non-small cell lung cancer (NSCLC) treated with EGFR tyrosine kinase inhibitors (TKIs). Here we report our experience.

Materials and methods. From May 2009 to March 2011, 90 pts underwent EGFR screening based on the presence of non-squamous histology. The main pts characteristics were: M/F 50/40; never-smokers 21%, former-smokers 50%, current-smokers 26%, not available 3%; stage IIIB 7%, IV 60%, recurrence 23%, other 10%; histology: adenocarcinoma 87%, poorly differentiated carcinoma 13%. The molecular analysis was performed with real-time PCR (kit TheraScreen DxS) and the DNA was extracted by kit Qiagen (QIAamp DNA FFPE tissue kit).

Results. EGFR mutations were detected in 18 (20%) pts: primarily exon 19 deletions (55.5%) and exon 21 L858R (39%), though 5.5% of mutation-positive cases had less common exon 20 insertions. The main EGFR-mutant pts characteristics were: women 67%, never-smokers 67%, adenocarcinoma 94%. First-line chemotherapy was administered in 68 (75.5%) pts: 58 (85.3%) were EGFR wild-type, whereas 10 (14.7%) were EGFR-mutant. The disease control rate (DCR) (CR + PR + SD) was 64% for EGFR-wt pts and 80% for EGFR-mutant; time-to-progression (TTP) was 4.5 and 6 months and overall survival (OS) was 8+ and 11.5+ months for EGFR-wt and EGFR-mutant respectively. TKI erlotinib monotherapy was administered in 10 (11.1%) pts: 60% were EGFR-wt and 40% EGFR-mutant. The DCR was zero for EGFR-wt pts and 75% for EGFR-mutant; TTP was 1+ and 10.5+ months and OS was 3.5 and 13.5+ months for EGFR-wt and EGFR-mutant respectively. TKI gefitinib monotherapy was administered in 14 (15.5%) EGFR-mutant pts, with a DCR of 72.7%; after a median follow-up of 5 months it's still too early for TTP and OS.

Conclusions. Our experience confirms the prognostic and predictive value of activating EGFR mutations. In spite of the small number of our series, these results suggest that the use of EGFR TKIs should be limited to NSCLC pts with EGFR mutations.

D59 THE ROLE OF INDUCTION CHEMOTHERAPY FOR THE TREATMENT OF LOCO-REGIONALLY ADVANCED NASOPHARYNGEAL CARCINOMA

Ferrari D.[1], Codecà C.[1], Bertuzzi C.[1], Crepaldi F.[1], Broggio F.[1], Luciani A.[1], Caldiera S.[1], Cossu Rocca M.[2], Alterio D.[3], Foa P.[1]

[1]U.O. Oncologia Medica, Ospedale San Paolo, Università di Milano; [2]Unità di Cure Mediche, Istituto Europeo di Oncologia, Milano; [3]Divisione di Radioterapia, Istituto Europeo di Oncologia, Milano

The role of induction chemotherapy (IC) followed by concomitant chemoradiotherapy (CRT) for the treatment of nasopharyngeal carcinoma (NPC) is not established yet. We designed a phase II study with the aim of evaluating the effectiveness and tolerability of such a program.

Thirty-six untreated patients (pts) with stage II-IVb NPC were included. IC consisted in 3 cycles of cisplatin (CDDP, 100 mg/m^2 i.v.) on day 1, and 5-fluorouracil (5-FU), 1000 g/m^2/day administered on days 1-4 as continuous intravenous infusion (PF regimen) or 3 cycles of CDDP (75 mg/m^2 i.v.) on day 1, docetaxel (75 mg/m^2 i.v) on day 1 and 5-FU (750 mg/m^2/d) administered on days 1-4 as continuous intravenous infusion (TPF regimen), both repeated every 3 weeks. During RT, CDDP was administered at a dose of 100 mg/m^2 intravenous infusion on days 1, 22 and 43, given 60 min before radiation. Eleven (30.6%) pts had stage II, 16 (44.4%) stage III, 6 pts (16.7%) stage IVa and the remaining 3 (8.3%) stage IVb disease. Males were 72.2%, the median age was 52 years. Of the 36 pts treated with IC, 31 (86.1%) received the PF regimen and 5 the TPF regimen.

At the end of the CRT, a CR was obtained in 30 pts (83.3%) and a PR in 6 pts (16.7%). At a median follow-up of 36 months 7 pts (19.4%) experienced recurrent disease, 4 loco-regional and 3 metastatic. One patient died after recurrence. Three-year progression-free survival and 3-year overall survival were 78.2% and 97.1%, respectively. During IC grade 3-4 neutropenia occurred in 4 patients (11.1%) and neutropenic fever in 2 patients (5.5%). Oropharyngeal mucositis occurred in all patients during CRT. Eleven (30.5%) developed a severe mucosal reaction (grade 3-4) with ulcers and transient inability in speech and swallowing, 3 developed grade 3 disgeusia and xerostomy. Two pts developed grade 3 neuropathy.

IC followed by concomitant CRT is effective and tolerable for pts with loco-regionally advanced NPC.

D60 RADIOFREQUENCY THERMAL ABLATION (RF) IN INOPERABLE STAGE I NON-SMALL CELL LUNG CANCER (NSCL): EXPERIENCE OF THE GROUP OF THORACIC PATHOLOGY-GENERAL HOSPITAL OF TREVISO

Cancian L.*, Lucernoni P.^, Dorigo A.*, Rosti G.°, Morana G.*

**U.O. Radiologia Diagnostica, ^U.O. Pneumologia, U.O. Oncologia, Ospedale Regionale di Treviso*

Aim. To assess feasibility and efficacy of RFA in NSCLC stage T1-T2a; define response criteria using CT in the follow-up.

Study design. Case histories retrospective assessment in our center.

Materials and methods. From 2005 to 2009 were treated 20 pts (16M/4F, age 61-84 yrs) with NSCLC (first diagnosis or relapse) in stage IA-B, non-operable for comorbidity. The treatments were performed with CT-guided percutaneous approach (needle multiprobe hook). Lesions >3 cm (7/20) were performed at 6 months with collimated radiation therapy. The follow-up CT scan was performed at 1, 3, 6, 12 months, then with annual CT.

Results. To assess treatment response were used RECIST 1.1 criteria associated with modified Choi criteria. The radiological response at 6 months was: complete or partial in 12/20 (60%), stability in 2/20 (10%), local or nodal progression in 6/20 (30%). With a follow-up of 24 months (evaluable in 16/20 pts), the survival rate was 86% at 1 year and 50% at 2 years.

Conclusions. The RF is indicated in inoperable early stage NSCLC, it is feasible even if it requires experience. In lesions <3 cm there is a good accuracy in the treatment of the margins, otherwise in lesions over 3 cm is useful the association with RT. The follow-up CT should be directed to assess the vascularity of the lesion, the size criterion alone is inadequate because the volume increases during the first 3-6 months due to coagulation necrosis. Although the CT/PET scan is the gold standard, the use in the follow-up of the MRI could be a good approach for the evaluation of vascularity and cell density into the treated lesion.

D61 PHASE II STUDY WITH WEEKLY SCHEDULE OF DOCETAXEL AND CISPLATIN IN PATIENTS WITH ADVANCED NSCLC

Gambaro A., Filipazzi V., Cattaneo M.T., Isabella L., Tosca N., Ferrario S., Fasola C., De Troia B., Farè E., Somma L., Mauceri A., Damiani E., Piazza E.

Oncology Department "Luigi Sacco" Hospital, Milan, Italy

Background. Docetaxel and cisplatin combination chemotherapy is established first-line chemotherapy for advanced non-small cell lung cancer (NSCLC)[1]. We evaluated a weekly schedule of docetaxel and cisplatin for efficacy and tolerability in chemo-naïve patients with NSCLC.

Patients and methods. From 2008 to 2010, 34 pts were enrolled, 26 males and 8 females, median age 67 years (range 62-75) with 30% over 70; ECOG PS was 0-1 in 23 pts and 2 in 11 pts. For histology 5 pts (15%) had ADK, 20 pts (57%) had SQM carcinoma while 9 pts (28%) had NSCLC (NOS). The clinical stages of disease were III b in 6 cases and IV in 28 pts. The sites of metastases were 4 liver, 5 brain, 8 bone, 10 lung and 4 pleural effusion.

All pts received chemotherapy with cisplatin 25 mg/m^2 + docetaxel 30 mg/m^2 day 1-8-15 every 28 days for 3 cycles. Patients were evaluated for response after 3 cycles of chemotherapy. Three other cycles were performed only in responder pts, that were evaluated for radiation too. Standard anti-emetic therapy was performed.

Results. All patients were evaluated for toxicity and efficacy. A total of 125 cycles were performed with average of 4 cycles for pt (range 1-6). The RR was 30% with 10 PR and 11 stable disease while 13 pts went in progression during chemotherapy. Nine responders underwent radiation therapy with 56 cGy on the thorax and 2 of them were resected.

The mTTP for responder pts was 5 months (range 2-24) and the MST was 9 months (range 4-24) with 6 pts alive over 24 months. The major grade 3/4 haematological toxicity consisted in neutropenia (12%), anemia (10%), emesis 10%; 4 cases of allergic reaction were recorded. Al grade nausea, alopecia and fatigue occurred in 35%, 55%, and 44% respectively.

Conclusions. The weekly combination of cisplatin and docetaxel was well tolerated and effective in first-line treatment for advanced NSCLC patients.

References

1. Tartarone A et al: Cisplatin and weekly docetaxel as first-line therapy in patients with advanced non-small cell lung cancer. Tumori, 91: 131-134, 2005.

D62 MULTIDISCIPLINARY APPROACH IN LUNG CANCER: GIPO (INTERDISCIPLINARY PNEUMO-ONCOLOGIC GROUP) EXPERIENCE

Monti M.[1], Zoli W.[1], Sanna S.[2], Polico R.[1], Poletti V.[3], Nanni O.[1], Minguzzi M.[1], Milandri C.[1], Matteucci F.[4], Maltoni M.[6], Giovannini N.[1], Gavelli G.[1], Dubini A.[5], Riva N.[1], Burgio M.A.[1], Amadori D.[1], Genestreti G.[1]

[1]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), Meldola; Unit of [2]Thoracic Surgery, [3]Pneumology, [4]Radiology and Nuclear Medicine, [5]Pathology, Morgagni-Pierantoni Hospital, Forlì; [6]Palliative Care Unit, Hospice, Forlimpopoli, Italy

Background. Lung cancer is the most common cause of cancer death in both men and women worldwide. Recent advances in diagnostic procedures, biomolecular pathways and innovative and tailored treatments have led to a more multidisciplinary management of patients.

Methods. The Interdisciplinary Pneumo-Oncologic Group (GIPO) was founded at IRST in May 2007 to improve the disease staging and care management of lung cancer patients. The group is coordinated by a medical oncologist in close collaboration with specialists in surgery, pneumology, radiotherapy, radiology, pathology, nuclear medicine, palliative care, biology, data manager and nurse. GIPO meetings are performed weekly and are divided into 2 parts: the first focuses on clinical patient evaluation by the team of specialists to formulate an individually-tailored diagnostic-therapeutic program. This work practice offers more effective relationships between primary care and specialists, and ensures an integrated approach to treatment decisions in a short, concentrated time period. An accurate patient database has been created that enables periodic statistical analysis on clinical outcomes, patient's satisfaction, and the quality of team work.

Results. From May 2007 until now, 942 patients have been discussed by the GIPO team, 57% of whom received chemotherapy, 20% surgery, 10% radiotherapy and only 6% palliative care. The median time from presentation to first treatment was 3 weeks. GIPO experience improved clinical trials accrual (20% of potential patients enrolled) and the design of new studies on imaging and diagnostic procedures (endobronchial ultrasound-EBUS and endoscopic ultrasound-EUS).

Conclusions. The GIPO approach offers more rapid and accurate diagnosis, optimization of time and cost resources, development of innovative strategy patterns, and utilization of new drugs in clinical trials. We plan to evaluate the impact on survival and quality of life data. Evidence of a multidisciplinary approach is unequivocable to improve patient management and quality of diagnosis and therapy.

D63 ERLOTINIB IN PRE-TREATED METASTATIC NSCLC PATIENTS

Isabella L., Filipazzi V., Cattaneo M.T., Gambaro A., Tosca N., Ferrario S., Fasola C., De Troia B., Somma L., Farè E., Mauceri A., Pellegrino P., Damiani E., Piazza E.

Oncology Department "Luigi Sacco" Hospital, Milan, Italy

Background. Erlotinib is an oral tyrosine kinase inhibitor usually used after chemotherapy in advanced lung cancer patients[1]. The aim of this study is to analyse retrospectively the outcome of unselected population affected by NSCLC treated with erlotinib after chemotherapy failure.

Patients and methods. We evaluated all pts with advanced NSCLC treated with erlotinib from 2007 in our institute, recording: gender, histology, age, PS by ECOG, line of treatment, objective response, time to progression and toxicity. Erlotinib was given at the standard daily dose of 150 mg p.o., but dose reductions were possible in case of toxicity.

Results. There were 69 pts, 33 males and 36 females, median age 73 years (range 45-85), 57 pts in PS 0-2, and 12 pts in PS 3-4, 36 ADK (52%) + 27 SQM (39%) and 6 NSCLC-NOS (9%). Erlotinib was the second-line treatment after chemotherapy in 14 pts (20%), the third-line in 40 pts (59%) while in 15 pts (21%) it was over the third one. Objective responses were observed in 11 pts (17%) (4 smoker males with SQM and 7 no smoker females with ADK); 18 pts experimented stable disease while 34 pts had pro-

gression disease within 3 months from starting TK inhibitor, while other 6 pts were not valuable because they stopped treatment for toxicity. The most common side effect was skin rash G1-2 (65%); grade 3-4 toxicity developed in 10 pts (1 bullos dermatosis, 2 cutaneous rash G4, 3 diarrhea G3, 3 renal failure and 2 epatic toxicity). mTTP in 29 (PR +SD) pts was 6.5 months; 4 pts are alive over 24 months from diagnosis and over 12 months after TKi.

Conclusion. In our experience erlotinib confirms his safety and mild efficacy in unknow mutation EGFr pts; the best control rate was recorded in no smoker females with ADK.

References

1. Cataldo VD et al: Treatment of non-small cell lung cancer with erlotinib or gefitinib. N Engl J Med, 364 (10): 947-955, 2011.

D64 FIRST-LINE MODIFIED SCHEDULE OF GEMCITABINE WITH A LOWER DOSE THAN STANDARD IN ELDERLY OR PS 2 PATIENTS WITH ADVANCED NSCLC

Nacci A., Mazzoni E., Rizzo P., Calvani N., Orlando L., Sponziello F., Schiavone P., Fedele P., Chetrì C., D'Amico M., Marino A., Cinefra M., Cinieri S.

U.O.C. Oncologia, Ospedale "Senatore Antonio Perrino", Brindisi, Italy

Background. Monochemotherapy with gemcitabine (Gem) is often the treatment of choice in elderly or poor performance status (PS) patients with advanced non-small cell lung cancer (NSCLC). Our study was aimed to assess the efficacy and tolerability of a modified schedule of Gem using a lower dose than standard.

Patients and methods. From May 2009 through December 2010, fifty patients (43 males and 7 females with a median age of 76 years ranging from 64 to 85) with advanced NSCLC (stage IIIB 34.0% and IV 66.0%) were enrolled. Histology was: squamous 39.6%, adenocarcinoma 31.2%, large cell 6.2%, undifferentiated 4.2%, undetermined 18.8%. Only eight patients (16.0%) had a WHO PS 0 whereas nineteen (38.0%) were PS 1 and eleven (46.0%) PS 2. All patients received first-line chemotherapy with 6 cycles of Gem 1000 mg/m^2 on days 1 and 8 every 4 weeks.

Results. At the time of analysis 35 patients were evaluable for response. Partial response (PR) was achieved in 7 patients (20.0%), stable disease >12 weeks (SD) in 16 (45.7%) whereas 12 had progressive disease (34.3%). Importantly, the clinical benefit rate (PR + SD) was 65.7%. Tumour markers (CEA and NSE) were high in 28 patients with a reduction in their values observed in 11 of them (39.3%). Both pain and PS improved in 6 patients (17.1%) whereas 19 (54.2%) had an improvement in pain with no worsening of PS. We observed only grade 2 WHO haematological toxicities including anemia, leucopenia, neutropenia and trombocytopenia. Not-neutropenic fever occurred in 4 patients (11.4%). Overall, we did not observe any not-haematological treatment-related event.

Conclusions. Our data show that a modified schedule of Gem with a lower dose intensity than standard may be beneficial in terms of both disease control and tolerability when employed in elderly or PS 2 patients with advanced NSCLC.

D65 TREATMENT OF MASSIVE HEMOPTYSIS BY BRONCHIAL ARTERY EMBOLIZATION: A CASE REPORT

Evangelista M.L., Bianchetti S., Maritati R., De Padua L., Bussa S., Brunetti M., Angelini F.

S.C. di Oncologia ed Ematologia, "Ospedale Regina Apostolorum", Albano Laziale, Roma

Background. Hemoptysis in patients with lung cancer is not uncommon and occurs in about 30% of patients.

It is usually mild, resulting in blood-streaked sputum, anyway in some patients can be life threatening and can delay the treatment of underlying disease.

Hemoptysis has been managed with various treatment options other than surgery and medicine, such as endobronchial tamponade, transcatheter arterial embolization and radiation therapy. However, these methods can sometimes be used only temporarily or are not suitable for all patient's condition.

Case report. We present a case of a 74-year-old man with uncontrollable hemoptysis caused by central lung cancer successfully treated by bronchial artery embolization (BAE).

The patient had a huge right pulmonary poorly differentiated carcinoma of the lung NOS diagnosed, in November 2010 without distant metastases.

From November 2010 to March 2011 he received six cycles of carboplatin AUC 5 day 1 and gemcitabine 1000 mg/m^2 day 1 and 8, every 21 days, obtaining a WHO criteria PR.

At the end of March 2011 he was admitted to our departement due to persistent hemoptysis.

A bronchoscopy was performed showing bronchial occlusion of the medial segment of right upper lobe by a necrotic neoplasia with signs of recent bleeding. A selective angiography showed bleeding from a branch of the right bronchial artery.

The subsequent therapeutic intervention consisted in a selective bronchial artery embolization.

The patient experienced an almost immediate reduction in the amount of bleeding persisting in the following days only as sputum streaked with blood.

Outcome of treatment was also evaluated with a CT scan showing increased necrosis of the right lung mass compared to the previous examination.

The patient was discharged in fair good general conditions that persist up now.

Conclusion. BAE may be a safe and effective procedure for the treatment of hemopthysis and could be regarded as a well-tolerated treatment option in this subset of patients.

D66 MALT LYMPHOMA OF PAROTID GLAND IN PREVIOUS TREATED PROSTATIC ADENOCARCINOMA AND SKIN SPINOCELLULAR CARCINOMA RELAPSES: A CASE REPORT

Sponghini A.[1], Rondonotti D.[1], Ritorna A.[1], Pia F.[2], Policarpo M.[2], Alabiso O.[1]

[1]S.C. Medical Oncology, [2]S.C. Otorinolaringoiatry, University of Piemonte Orientale "Amedeo Avogadro", Hospital "Maggiore della Carità", Novara

A 81-years-old male presented in February 2010 for ulcerated indolent lesion of left temporal area. In his past medical history

were relevant radical prostatectomy and lymphoadenectomy for adenocarcinoma pT3 pN1 GS 8 followed by adjuvant pelvic radiotherapy in 2001 and excision of a G2 spinocellular carcinoma of scalp in September 2008, with local recurrence of G3 spinocellular carcinoma in December 2008 and May 2009 undergone excisions.

Facial TC performed on March 2010 showed cutaneous and subcutaneous ulceration in left temporal area with lymphadenopathies in lateral cervical node chains. Patient underwent on April 2010 lateral cervical lymph nodes dissection, left total parotidectomy and removal of a temporal skin island containing the neoplasm. Histological analysis showed small B-cell lymphoma cells in twenty-five lymph nodes. A G2 squamous cell carcinoma involving the parotid was detected and the skin overlying the parotid was positive for presence of B-cells. Subsequent bone marrow biopsy showed small B-cell lymphoma NOS and immunophenotyping of peripheral blood appeared to be consistent with NHL, CD5 positive.

Considering histotype, and absence of clinical symptoms and patient's age we proceed with exclusive follow-up.

In November 2010 a left fixed lateral cervical was detected, so patient underwent radical left lateral cervical emptying. Histological analysis evidenced infiltration by poorly differentiated squamous cell carcinoma of skin, derma extended to skeletal muscle. Thirteen out of fifteen lymph nodes showed the presence of poorly differentiated adenocarcinoma and neoplastic infiltration of the connective/adipose tissues surrounding the lymph nodes.

Immunochemistry tests performed with anti-PSA antibody indicated prostatic origin of neoplasm, while morphological alterations of residual lymph nodes areas were indicative of a diffuse B-cell malignant lymphoma.

TC-PET performed in December 2010 showed no pathologic uptake in except for the area involved in recent surgery.

Taking account of the local stage of disease, age and overall clinical patient's conditions we decided to start total androgenic ablation and a wait and see approach.

D67 EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) G719C MUTATION AS NEW DETERMINANT OF LONG TERM SURVIVAL AND RESPONSE IN PATIENTS WITH NON-SMALL CELL LUNG CANCER TREATED WITH ERLOTINIB: A CASE REPORT

Franchina T., Proto C., Noto L., Chiofalo G., Ferraro G., Picciotto M., Adamo V.

Unit of Integrated Therapies in Oncology, Department of Human Pathology, University of Messina, Italy

Objective. The G719C mutation occurs within exon 18 and has been associated with increased sensitivity to TK inhibitors, particularly to gefitinib (Han SW, 2005; Lynch TJ, 2004; Rosell R, 2005) and neratinib (Sequist LW, 2010). This case report aims to highlight the interesting role of this mutation in erlotinib treatment.

Design and method. We report a case of a 67-year-old smoker man, affected by metastatic NSCLC. In March 2005 he underwent a left lower lobectomy for adenocarcinoma G3 (stage T2 N1 M0). No adjuvant therapy was performed for a low LVEF. A computed tomography (CT) assessment performed three months later showed disease progression with the appearance of a brain metastasis, treated with radiosurgery. Then he was treated with carboplatin based chemotherapy. Five months after chemotherapy, CT scan showed lung disease progression with mediastinal nodal involvement. Mediastinal radiotherapy was performed, obtaining a stable disease. A second-line was planned.

Results. Exons 18 to 21 of EGFR gene were sequenced and a missense mutation in exon 18 (G719C) was identified in tumour DNA.

In August 2008 the patient arrived at our observation and was commenced on EGFR inhibitor erlotinib at the dose of 150 mg daily. A chest CT, performed two months after erlotinib treatment, showed a marked resolution of lung mass, confirmed at the subsequent CT controls. We recorded only a grade 1 dry skin.

At the last follow-up 57 months after starting erlotinib, the patient remains in complete remission, as evidenced by negative whole body CT scan.

Decision to continue erlotinib treatment was made jointly with the patient because of the risk of relapse and the hypothesis of a rebound progression after withdrawal of erlotinib, as described in literature.

Conclusions. Although preclinical models and previous studies showed that erlotinib may be more selective for exon 19 deletion mutations, G719C mutation should represent an important determinant of survival and response, highlighting the importance of obtaining comprehensive genetic information on targeted agents.

D68 FIRST-LINE TREATMENT OF ADVANCED NON-SMALL CELL LUNG CANCER WITH CARBOPLATIN PLUS PEMETREXED: A PHASE II STUDY IN OUR INSTITUTION

Duluc M., Cotroneo G., Bonassi L., Mauri C., Iaculli A., Galdy S., Rodà G., Nastasi G.

U.O. Oncologia Medica, A.O. Bolognini, Seriate (BG)

Background. For a long time, the standard of care for chemonaïve patients with advanced NSCLC has been a platinum-based chemotherapy doublet. However, none of these platinum-based doublets provides a clear survival advantage. In July 2004, on the basis of the response data from several trials, pemetrexed received accelerated approval by the FDA for the treatment of non-small cell lung cancer (non squamous histology).

Aim. The primary objective of this study was to determine the efficacy and tolerability of a pemetrexed-carboplatin combination as first-line therapy in patients with advanced non-small cell lung cancer.

Patients and methods. From February 2008 to January 2010 we enrolled 15 eligible patients (pts) with histologically documented stage IIIB (malignant effusion) or IV NSCLC (non squamous) with a Karnofsky performance status of 90 or 80, absence of brain metastases and measurable disease as defined by the RECIST criteria. Treatment was pemetrexed 500 mg/m^2 given intravenously and carboplatin (AUC 5) given intravenously on day 1 every 3 weeks for six cycles; patients could receive additional cycles at the discretion of the physician and patient. All patients received folic acid, vitamin B12 and dexamethasone prophylaxis.

Results. Fifteen patients (8 men and 7 women) were treated. The median age was 58 years (range 52-70); 83% of patients had stage IV disease, and 75% had a performance status of 80 (KPS). The median number of cycles was 6. There was grade 3/4 neutropenia in 3 (20%) and 1 (6%) patients, respectively; grade 3 thrombocytopenia in 4 (27%). Three patients (20%) experienced grade 3 non-hematologic side effects (diarrhea, vomiting and fatigue). No patients had sensory neuropathy or alopecia >grade 1. The partial response rate was 22.4%.

Conclusions. This is an active regimen in treating advanced non squamous lung carcinoma and has an acceptable toxicity profile.

D69 CETUXIMAB IN THE TREATMENT OF RECURRENT OR METASTATIC SQUAMOUS CELL CARCINOMA OF HEAD AND NECK: OUR INSTITUTIONAL EXPERIENCE IN 20 CASES

Marra L., Rocchi A., Conte P.F.

Oncology, Haematology and Respiratory Diseases Department, University Hospital of Modena, Modena, Italy

Purpose. We report the efficacy of cetuximab administered as a single agent or in combination with chemotherapy or radiotherapy in recurrent/metastatic squamous cell carcinoma of head and neck (SCCHN).

Patients and methods. From March 2006 to July 2010 we have treated 20 patients (pts) (14 M/6 F), with recurrent/metastatic SCCHN. Median age was 61 yrs (39-79). Performance status was 0-1 in 11 pts, ≥2 or more in 9 pts. Primary tumours were in oropharynx in 2 pts, larynx in 10 pts, oral cavity in 6 pts, nasopharynx in 2 patients. 13/20 pts had locally recurrent disease and 7/20 pts had metastatic disease. Cetuximab was administered alone in 3/20 pts in first-line; with chemotherapy in 17/20 pts (in 12 pts as first-line, in 5 pts as ≥2nd line) according to the following regimens: carboplatin/fluorouracil 1 pt; cisplatin/fluorouracil 8 pts; cisplatin 3 pts; navelbine 2 pts; carboplatin/navelbine 1 pt; cisplatin/taxotere 1 pt; carboplatin 1 pt. Standard radiotherapy plus concomitant cetuximab was applied in 2 pts with local recurrent squamous cell carcinoma of the larynx and in 1 case of lateral-cervical lymph nodes recurrent oral cavity carcinoma.

Results. The addiction of cetuximab did not change the tolerability profile of the chemotherapy regimens and no chemotherapy or radiotherapy dose reductions were needed. Grade 1-2 skin toxicities were observed in 7/20 pts. Mean overall duration of treatments was 22.6 weeks (1-93 weeks); in nasopharynx carcinoma the mean duration of treatment was 34.4 weeks (6-63 weeks). A disease control was achieved in 57% of the patients. Median progression-free survival was 5.4 months (interval: 1-13.5 months, only pts treated in first-line setting). Overall survival was 10.1 months (2-24.66 months).

Conclusions. The administration of cetuximab with chemotherapy or radiotherapy is an effective and tolerable option in recurrent/metastatic nasopharynx cancer.

Session E • Colorectal cancers

E1* KRAS MUTATIONS IN COLORECTAL CANCER PATIENTS: RESULTS FROM THE *KRAS* aKtive PROGRAM

Marchetti A., Pinto C., Taddei L., Troncone G., Russo A., Fontanini G., Larocca L.M., Mottolese M., Giannini G., Ruco L., Roz E., Scarpa A., Calabrese G., Bortesi B., Vaccarella S., Cossu A., Ludovini V., Normanno N.

Università "G. D'Annunzio", Chieti; Ospedale S. Orsola Malpighi, Bologna; Università di Firenze; Università Federico II, Napoli; Università di Palermo; Università di Pisa; Università Cattolica del Sacro Cuore, Roma; Istituto Tumori Regina Elena, Roma; Università La Sapienza, Roma; Azienda Ospedaliera Sant'Andrea, Roma; Casa di Cura la Maddalena, Palermo; Università di Verona; Ospedale Civile di Pescara; Azienda Ospedaliera di Parma; Presidio Ospedaliero Mariano Santo, Cosenza; Azienda Ospedaliero-Universitaria di Sassari; Ospedale S. Maria Della Misericordia, Perugia; I.N.T. Fondazione G. Pascale, Napoli

The Italian Association of Medical Oncology (AIOM) and the Italian Society of Surgical Pathology and Cytopathologyy (SIAPEC) collaborated to the promotion of a national program (*KRAS* aKtive) to support the activity of oncologists and pathologists involved in the management of metastatic colorectal cancer patients who need the assessment of the mutational status of the *KRAS* gene. The *KRAS* aKtive program was specifically devised to facilitate the exchange of biologic material, clinicopathological data and diagnostic reports within a network of oncologists, pathologists and pathology/molecular biology reference laboratories throughout Italy, connected through the site www.kras-aKtive.it.

KRAS mutation analysis was performed by PCR-Sanger sequencing, real time PCR or other techniques. Data were collected in a common database. Started on March 2009, the *KRAS* aKtive program has involved 433 oncologists, 133 pathologists, and 27 reference laboratories from 16 Italian regions.

A total of 5323 *KRAS* mutations texts were performed. The tests were informative in 5198 (97.6%) cases. The vast majority of informative tests (4179 cases, 80.4%) were conducted by sequencing. In 373 (7.2%) cases a real-time PCR assay was used, other detection techniques were used in 646 (12.4%) cases. *KRAS* mutations at codons 12-13 were detected in 2035 (39.1%) cases. The frequency of mutations detected by sequencing was lower than that observed by real-time PCR (37.6 and 47.7%, respectively). The frequency of the different type of mutations at codons 12 and 13, evaluated by sequencing, is reported in Table 1.

The results of this large survey allow an accurate estimation of the actual prevalence of *KRAS* mutations and their types in Caucasian colorectal cancer patients. Moreover, although the subset numbers are still insufficient to draw definitive conclusions, our data suggest that the frequency of mutations detected by real-time PCR amplification is higher than that obtained by sequencing. Program supported by Merck Italy.

Table 1

Mutation type	Number	%
GGT->GTT G12V	412	26.19
GGT->GAT G12D	482	30.64
GGC->GAC G13D	308	19.58
GGT->TGT G12C	128	8.14
GGT->GCT G12A	96	6.10
GGT->AGT G12S	86	5.47
GGT->CGT G12R	23	1.46
Other	38	2.42
Total	1573	100.00

E2* LET-7A MICRO-RNA LEVELS IN *KRAS* MUTATED COLORECTAL CARCINOMAS IMPACT ON SURVIVAL OF PATIENTS TREATED WITH SALVAGE CETUXIMAB

Ruzzo A.[1], Vincenzi B.[2], Canestrari E.[1], Perrone G.[3], Galluccio N.[1], Lorenzini P.[4], Rulli E.[5], Catalano V.[6], Loupakis F.[7], Bisonni R.[8], Rabitti C.[3], De Nictolis M.[4], Santini D.[2], Salvatore L.[7], Tonini G.[2], Giustini L.[8], Falcone A.[7], Magnani M.[2], Graziano F.[6]

[1]Department of Biomolecular Sciences, University of Urbino, Italy; [2]Medical Oncology Unit, University Campus Bio-medico, Rome, Italy; [3]Department of Anatomical Pathology, University Campus Bio-medico, Rome, Italy; [4]Institute of Histopathology, Azienda Ospedaliera "Ospedali Riuniti Marche Nord", Pesaro, Italy; [5]Laboratorio Clinical Trials, Istituto di Ricerche Farmacologiche "Mario Negri", Milan, Italy; [6]Department of Onco-Hematology, Division of Medical Oncology, Azienda Ospedaliera "Ospedali Riuniti Marche Nord", Pesaro, Italy; [7]Unità Operativa Oncologia Medica Universitaria, Azienda Ospedaliero-Universitaria Pisana, Istituto Toscano Tumori, Pisa, Italy; [8]Medical Oncology Unit, Hospital of Fermo, Italy

Background. Lack of alternative salvage treatment strategies for patients with metastatic colorectal cancer (CRC) harboring *KRAS* mutations makes this setting of particular interest for translational research. The *Let-7* microRNA post-transcriptionally down-regulates *KRAS*, and exogenous *Let-7* reduced tumour formation in animal models expressing activating *KRAS* mutation. We hypothesized the existence of a proportion of CRC patients with *KRAS* mutation who may still obtain survival benefit from anti-EGFR therapy when their tumours display up-regulated *Let-7* levels. Therefore, we quantified the *Let-7a* isoform in colorectal carcinomas with *KRAS* mutations and in patients treated with salvage cetuximab-irinotecan. The *Let-7a* levels were characterized and studied for association with survival outcomes.

Methods. The study population was retrospectively identified among metastatic CRC patients who underwent third-line cetuximab/irinotecan in a period when epidermal growth factor receptor (EGFR) expression only was required for adopting the anti-EGFR therapy. In 59 patients harboring *KRAS* mutations, *Let-7a* levels were analyzed for association with overall survival (OS) and progression-free survival (PFS). An exploratory subgroup analysis was performed according to the rs61764370 (*LCS6* T >G) single nucleotide polymorphism that experimentally impairs the *Let-7* binding to the *KRAS* mRNA.

Results. Increased *Let-7a* levels were significantly associated with improved survival (Hazard Ratio = 0.88; 95% CI = 0.79-0.98; p = 0.02). In the exploratory analysis of the 45 *LCS6* wild-type patients (excluding 14 *LCS6* G allele carriers), there was a significantly favorable association between high *Let-7a* and both OS (Hazard Ratio = 0.86; 95% CI = 0.76-0.96; p = 0.01) and PFS (Hazard Ratio = 0.87; 95% CI = 0.78-0.98; p = 0.02). All associations were confirmed in the multivariate model. Grade 2-3 skin toxicity occurred more frequently in cases with high *Let-7a* levels (p = .002). Results did not change after excluding ten patients with *KRAS* codon 13 mutations.

Conclusions. These results may lead to novel perspectives in the overall treatment strategy of KRAS mutated CRC patients. Up-regulated *Let-7* may qualify a proportion of patients with *KRAS* mutation who obtain survival benefit from anti-EGFR therapy. Also, they may encourage the development of innovative therapeutics that mimic microRNAs functions.

E3* THE ROLE OF BEVACIZUMAB (B) IN THE MAINTENANCE TREATMENT AFTER CHEMOTHERAPY (CT) FOR METASTATIC COLORECTAL CANCER (MCRC) PATIENTS (PTS): AN ITALIAN MULTICENTER RETROSPECTIVE ANALYSIS

Moscetti L.[1], Fabbri A.[1], Sperduti I.[2], Pochesci A.[3], Alesini D.[3], Gemma D.[4], Grande R.[5], Pavese I.[5], Franco D.[6], Ruggeri E.[1]

[1]U.O.C. Oncologia, Ospedale Belcolle AUSL Viterbo, Italy; [2]Biostatistics Regina Elena National Cancer Institute, Rome, Italy; [3]Division of Medical Oncology, Policlinico Umberto I, Rome, Italy; [4]Medical Oncology Unit, ASL Frosinone, Frosinone, Italy; [5]U.O.C. Oncologia Ospedale San Pietro Fatebenefratelli, Rome, Italy; [6]UOSA Oncologia ASL RM/A, Rome, Italy

Background. Maintenance treatment with B is considered an option for pts with mCRC responding to a first-line CT+B, but few data are available on its benefit on progression-free survival (PFS).

Methods. The clinical charts of 220 pts with mCRC pts treated with CT+B were reviewed. All the pts achieving a complete or partial response (CR or PR) or a stable disease (SD) were considered for the analysis. 118 pts received maintenance B (BM), whereas 102 did not (noBM). CR/PR or SD have been observed in 56% and 34% of pts in the BM group vs 49% and 31% in the noBM group. The median number of BM cycles administered was 7 (range 3-25). The Cox multivariate analysis was used to estimate the PFS on the entire population comparing BM and noBM and by response to prior CT+B (PR and CR versus SD).

Results. At a median follow-up of 18 months (1-109), the median PFS was 13 months (95% CI 11-15) vs 8 months (95% CI 7-10; p <0.0001, and the 1-year PFS 53% vs 28% for BM and noBM respectively. Patients with CR/PR had a mPFS of 15 months (95% CI 12-19) vs 10 months (95% CI 10-12) p = 0.004, and a 1-year PFS of 62.6% vs 33.7% for the BM vs noBM group respectively. No difference in the 1-year PFS was observed in pts showing SD to CT + B. The mPFS in these pts was 12 (95% CI 10-13) vs 8 months (95% CI 7-10, p = 0.11) for the BM and noBM group respectively. The multivariate analysis did not show any difference in PFS comparing age, sex, number and site of metastasis, k ras status. A significant difference in PFS was observed for response to first-line CT (CR/PR vs SD, p = 0.002) and for BM vs noBM (p = 0.003).

Conclusion. The maintenance strategy with B shows a longer PFS in pts responding or stable pts to the first-line chemotherapy + B.

E4* ANALYSIS OF HER-3, INSULIN-GROWTH FACTOR-1 (IGF-1), NUCLEAR FACTOR k-B (NF-kB) AND EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) GENE COPY NUMBER (GCN) IN THE PREDICTION OF CLINICAL OUTCOME FOR K-RAS WILD TYPE COLORECTAL CANCER PATIENTS RECEIVING IRINOTECAN-CETUXIMAB

Giampieri R.[2], Scartozzi M.[1], Maccaroni E.[2], Mandolesi A.[3], Giustini L.[4], Silva R.R.[5], Zaniboni A.[6], Biscotti T.[3], Biagetti S.[3], Galizia E.[5], Berardi R.[1], Loupakis F.[7], Falcone A.[7], Bearzi I.[3], Cascinu S.[1]

[1]Clinica di Oncologia Medica, AO Ospedali Riuniti, Ancona, Italy; [2]Scuola di Specializzazione in Oncologia, [3]Anatomia Patologica, Università Politecnica delle Marche, Ancona, Italy; [4]Oncologia Medica, Ospedale di Fermo, Italy; [5]Oncologia Medica, Ospedale Profili, Fabriano, Italy; [6]Oncologia Medica, Fondazione Poliambulanza, Brescia, Italy; [7]Oncologia Medica, Azienda Ospedaliera Pisana, Università di Pisa, Pisa, Italy

Background. A large proportion of colorectal cancer patients does not benefit from the use of anti-EGFR treatment although in the absence of a mutation of the K-RAS gene. Preliminary observations suggested that HER-3, IGF-1, NF-kB and EGFR GCN might identify patients not likely to benefit from anti-EGFR therapy. We tested the interaction between HER-3, IGF-1, NF-KB, EGFR GCN and K-RAS mutational analysis to verify the relative ability of these variables to identify a subgroup of patients more likely to benefit from EGFR-targeted treatment among those harbouring a K-RAS wild type status.

Patients and methods. We retrospectively collected tumours from 168 patients with metastatic colorectal cancer patients treated with irinotecan-cetuximab. K-RAS was assessed with direct sequencing, EGFR amplification was assessed by chromogenic in situ hybridization and HER-3, IGF-1 and NF-kB were assessed by immunoistochemistry.

Results. In patients with K-RAS wild type tumours, the following molecular factors resulted independently associated with response rate: HER-3 (OR = 4.6, 95% CI 1.8-13.6, p = 0.02), IGF-1 (OR = 4.2, 95% CI 2-10.2, p = 0.003) and EGFR GCN (OR = 4.1, 95% CI 1.9-26.2, p = 0.04). These factors also independently correlated with overall survival as follows: HER-3 (HR = 0.4, 95% CI 0.28-0.85, p = 0.008), IGF-1 (HR = 0.47, 95% CI 0.24-0.76, p <0.0001) and EGFR GCN (HR = 0.59, 95% CI 0.22-0.89, p = 0.04).

Conclusion. We believe that our data may help further composing the molecular mosaic of EGFR resistant tumours. The role of HER-3, IGF-1 and CISH EGFR GCN should be prospectively validated in clinical trials investigating anti-EGFR treatment strategies in colorectal cancer patients.

E5* DISCONTINUATION OF BEVACIZUMAB AND FOLFIRI ADMINISTERED UP TO A MAXIMUM OF 12 CYCLES IN FIRST-LINE METASTATIC COLORECTAL CANCER: A RETROSPECTIVE ITALIAN STUDY

Rosati G.[1], Cordio S.[2], Aprile G.[3], Butera A.[4], Avallone A.[5], Di Lucca G.[6], De Pauli F.[3], Soto Parra H.[2], Reggiardo G.[7], Bordonaro R.[2]

[1]Medical Oncology Unit, S. Carlo Hospital, Potenza; [2]Medical Oncology Unit, Garibaldi Hospital, Catania; [3]Department of Medical Oncology, University Hospital, Udine; [4]Medical Oncology Unit, S. Giovanni di Dio Hospital, Agrigento; [5]Department of Gastrointestinal Medical Oncology, National Cancer Institute, Naples; [6]Medical Oncology Unit, Civil Hospital, Saronno; [7]Biostatistic Unit Medi Service, Genova, Italy

Background. Bevacizumab significantly improves overall survival (OS) and progression-free survival (PFS) when added to chemotherapy for metastatic colorectal cancer (mCRC). A recent pooled analysis does not support a decreased time to disease progression, increased mortality, or altered disease progression pattern after cessation of bevacizumab therapy.

Patients and methods. PFS and OS were retrospectively analyzed in 209 mCRC patients discontinuing bevacizumab 5 mg/kg

and standard FOLFIRI regimen (leucovorin, infusional fluorouracil and irinotecan) as a result of any reason and administered up to a maximum of 12 cycles.

Results. At the time of the clinical cut-off for the analysis (31 March, 2010), the median duration of follow-up was 24 months. Median PFS was 10.7 months (95% CI 9.2-12.2 months). Fifty-five (26.3%) patients received at least 6 administrations and 114 (54.5%) of them received a maximum of 12 administrations of bevacizumab. Median OS reached 31.6 months (95% CI 25.8-37.3 months). Approximately 65% and 30% of patients received some form of second- and third-line therapy, respectively. Overall response rate was 49.8% (95% CI 42.9-56.6) and the disease control rate 81.8%. The most common grade 3-4 adverse events included neutropenia, diarrhea, fatigue and venous thromboembolic events. The toxicity profile of bevacizumab was consistent with that documented in previous trials.

Conclusions. This retrospective analysis does not support a decreased time to PFS or increased mortality after cessation of bevacizumab therapy in mCRC patients.

E6* HISTOPATHOLOGICAL RESPONSE TO FOLFOXIRI PLUS BEVACIZUMAB OF LIVER METASTASES FROM COLORECTAL CANCER

Schirripa M.[1], Loupakis F.[1], Caparello C.[1], Funel N.[2], Pollina L.[3], Vasile E.[1], Cremolini C.[1], Salvatore L.[1], Masi G.[1], Fornaro L.[1], Campani D.[4], Falcone A.[1]

[1]U.O. Oncologia Medica 2, Azienda Ospedaliero-Universitaria Pisana, Istituto Toscano Tumori, Pisa, Italy; [2]U.O. Chirurgia Generale e dei Trapianti nell'Uremico e nel Diabetico, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy; [3]Dipartimento di Medicina di Laboratorio e Diagnosi Molecolari, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy; [4]U.O. Anatomia Patologica Sperimentale, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy; Division of Medical Oncology, Department of Oncology, Transplants and New Technologies in Medicine, University of Pisa, Pisa, Italy

Background. Recent studies associated the histopathological response to chemotherapy with an improvement of prognosis for patient with colorectal liver metastases (CLM). An intensive treatment such as the FOLFOXIRI regimen produces a high rate of radiological and histopathologic responses. The contribution of bevacizumab added to chemotherapy in terms of tumoral shrinkage is a controversial issue, but it has been suggested that it might improve pathological regression of CLM. We investigated the effect of bevacizumab in addition to FOLFOXIRI on the pathologic response of CLM.

Methods. Forty-two patients enrolled in phase II or III clinical studies investigating FOLFOXIRI/XELOXIRI (n = 18) or FOLFOXIRI plus bevacizumab (n = 24) who underwent secondary resection of liver metastases were selected on the basis of tissue samples availability. Pathologic response in terms of tumour regression grade (TRG), and toxicity in the surrounding normal liver tissue were assessed according to previously reported criteria (briefly, regression grading spans from TRG 1, indicating complete response and absence of tumour cells to TRG 5, indicating no response and abundance of tumor cells). TRG was correlated with outcome.

Results. Fifteen (63%) of 24 patients treated with FOLFOXIRI plus bevacizumab showed a histopathological response (TRG 1, 2 or 3), while 5 (28%) of 18 patients treated with chemo only showed a TRG 1, 2 or 3 (p = 0.03). No significant difference in terms of pCRs was detected (4/24 (17%) vs 2/18 (11%), p = 0.69). The incidence of sinusoidal dilation and of liver steatosis was superimposable in the two groups. In the overall population (n = 42), patients with TRG 1, 2 or 3 achieved a median PFS of 39.5 vs 15.7 months of patients with TRG 4 or 5 (HR = 0.50, 95% CI 0.23-1.10, p = 0.08). The same comparison restricted to patients treated with FOLFOXIRI plus bevacizumab produced a significant difference (37.5 vs 14.1 months, HR = 0.29, 95% CI 0.06-0.82, p = 0.02).

Conclusions. The addition of bevacizumab to FOLFOXIRI improved pathologic response of CLM. TRG correlated with prognosis.

E7 BEVACIZUMAB (BEV) IN THE ADJUVANT TREATMENT OF HIGH-RISK STAGE III COLON CANCER: THE "TOSCA" EXPERIENCE (AIFA STUDY - FARM5RWTWZ)

Labianca R.[1], Sobrero A.[2], Montesarchio V.[3], Frustaci S.[4], Cortesi E.[5], Di Bartolomeo M.[6], Boni C.[7], Mucciarini C.[8], Galli F.[9], Rota S.[10], Frontini L.[10]

[1]Ospedali Riuniti, Bergamo; [2]A.O. San Martino, Genova; [3]A.O.R.N. dei Colli, P.O. Cotugno, Napoli; [4]C.R.O. IRCCS, Aviano (PD); [5]Policlinico Umberto I, Roma; [6]Fondazione INT, Milano; [7]Arcispedale Santa Maria Nuova, Reggio Emilia; [8]Ospedale Ramazzini, Carpi (MO); [9]IRFMN, Milano; [10]Fondazione GISCAD per la Ricerca sui Tumori, Parabiago (MI)

Background. After the presentation at 2006 ASCO Meeting of the MOSAIC study results, FOLFOX-4 regimen became the new standard of care for colorectal cancer (CRC) patients in adjuvant setting. At that time the risk-benefit profile of the bevacizumab (BEV) addition to the FOLFOX-4 regimen was unclear even if under evaluation in ongoing randomized controlled trials.

Methods. TOSCA (Three Or Six Colon Adjuvant) is an Italian, multicenter, open-label, randomized, phase III study conducted in radically resected stage II/III CRC patients to assess whether a 3-month adjuvant treatment with FOLFOX-4 is not inferior to a 6-month (duration study) one.

Once randomized in the duration study, in patients at high-risk stage III a second randomization with a 1 BEV: 3 no treatment ratio (emended in February 2010 to 1:1) could be done to assess the benefit of the BEV addition (5 mg/kg/iv infusion every 2 weeks for 6 months) to FOLFOX-4 (BEV study). Primary endpoint for both studies was relapse-free survival. In BEV study, the superiority hypothesis required 390 events in order to detect a hazard ratio of 0.75, with 2-sided 5% significance level and a 80% power.

Results. Started in June 2007, the BEV study was prematurely closed in December 2010 incorporating the recommendation of Data Safety Monitoring Committee following the negative results of the NSABP C-08 and AVANT trials. 181 patients (58 FOLFOX-4/BEV and 123 FOLFOX-4/no treatment) were randomized by 50 centers. Up-to-now data are available for 93% of patients.

At April 2011 with a median follow-up of 17.9 months, 33 patients relapsed and 6 died, accounting for 34 events. Treatment was completed in 64% and 84% of patients, interrupted in 23% and 15% and never started in 14% and 1% in FOLFOX-4/BEV and FOLFOX-4/no treatment, respectively. The main grade 3/4 toxicity were non-febrile neutropenia 30% and 25%, anemia 77% and 71%, cardiotoxicity 6% and 0% in FOLFOX-4/BEV and

FOLFOX-4/no treatment, respectively.

Patients are still being followed-up.

E8 PRELIMINARY RESULTS FROM A PHASE II STUDY OF PANITUMUMAB (P) IN COMBINATION WITH FOLFOXIRI AS FIRST-LINE TREATMENT OF MOLECULARLY SELECTED METASTATIC COLORECTAL CANCER (MCRC) PATIENTS (PTS)

Fornaro L.[1], Loupakis F.[1], Lonardi S.[2], Masi G.[1], Salvatore L.[1], Cremolini C.[1], Schirripa M.[1], Bergamo F.[2], Cappetta A.[2], Fontanini G.[3], Sensi E.[3], Lupi C.[3], Morvillo M.[1], Andreuccetti M.[1], Zagonel V.[2], Falcone A.[1]

[1]Azienda Ospedaliero-Universitaria Pisana, U.O. Oncologia Medica 2 Universitaria, Istituto Toscano Tumori, Pisa, Italy; [2]Istituto Oncologico Veneto, IRCCS, U.O.C. Oncologia Medica 1, Padova, Italy; [3]Anatomia Patologica Sperimentale, Università di Pisa, Istituto Toscano Tumori, Pisa, Italy

Background. GONO-FOLFOXIRI demonstrated higher activity and efficacy compared to FOLFIRI. P with oxaliplatin- or irinotecan-based doublets is feasible and associated with improved activity in *KRAS* codon 12-13 wild-type pts. *BRAF* and other *RAS* rare mutations have been suggested as additional potential biomarkers for anti-EGFR agents.

Material and methods. The GONO group is conducting a phase II trial to evaluate P 6 mg/kg d1 with a modified GONO-FOLFOXIRI regimen in pts with untreated unresectable mCRC and wild-type status for *BRAF-RAS* genes. The trial started with irinotecan 150 mg/m^2 d1, oxaliplatin 85 mg/m^2 d1, l-LV 200 mg/m^2 d1 and 5FU 3000 mg/m^2 48-h continuous infusion starting on d1 every 2 weeks. Protocol was amended because G3-4 toxicity in 2 out of first 3 pts enrolled and 5FU dose was reduced to 2400 mg/m^2.

Results. To date 46 pts have been screened and 20 pts enrolled. Main pts characteristics are: M/F, 50%/50%; median age (range) 61 (33-72) years; ECOG PS 0/1, 75%/25%; primary colon/rectum, 65%/35%; primary on site, 60%; sites of disease single/multiple, 35%/65%; liver only mts, 30%. So far 16 pts have received ≥4 cycles of chemotherapy and are assessable for toxicity. Among the first 3 pts treated with 5FU 3000 mg/m^2, 2 experienced SAEs (1 G4 diarrhea and febrile neutropenia; 1 G3 diarrhea). After amendment, maximum G3-4 per patient toxicities were: neutropenia, 38% (1 febrile neutropenia); diarrhea, 23%; stomatitis, 15%; neurotoxicity, 8%; cutaneous rash, 15%. Sixteen out of 81 cycles were delayed, mainly (9/56%) because of toxicity. One SAE (febrile neutropenia and sepsis) resulting in patient death occurred after amendment. Fourteen pts have been evaluated for response: we observed 11 PR (ORR: 79%) and 3 SD (disease control rate: 100%).

Conclusions. Adding P to GONO-FOLFOXIRI appears feasible, but requires a modest reduction in irinotecan and 5FU doses to improve gastrointestinal tolerability. After amendment, toxicity profile is acceptable and preliminary results in terms of activity are promising. Updated results will be presented.

E9 CONCORDANCE BETWEEN RM AND CT/EUS STAGING IN LOCALLY ADVANCED RECTAL CANCER (LARC): A BOLOGNA MULTIDISCIPLINARY RECTAL CANCER GROUP EXPERIENCE

Pini S.[1], Pinto C.[1], Di Fabio F.[1], Di Tullio P.[1], Cuicchi D.[2], Lecce F.[2], Golfieri R.[3], Ugolini G.[2], Iacopino B.[4], Rojas Llimpe F.L.[1], Giaquinta S.[1], Martoni A.

[1]Medical Oncology Unit, [2]Surgery Unit, [3]Radiology Unit, [4]Radiotherapy Unit, S. Orsola-Malpighi Hospital, Bologna, Italy

Background. In LARC staging assessment is important for decision-making in the treatment plan. Pelvic magnetic resonance (MR) is the gold standard for loco-regional disease assessment. The aim of this study is to compare endorectal ultrasound (EUS) and computed tomography (CT) with MR in LARC staging.

Methods. The Bologna Multidisciplinary Rectal Cancer Group of Sant'Orsola-Malpighi Hospital, made up of medical oncologists, medical radiotherapists, oncological surgeons, radiologists, nuclear physicians and pathologists evaluate patients (pts) with low/middle LARC. At diagnosis pts performed staging assessment with pelvic MR, EUS and CT. All patients with cT3-4 and/or N+ stage received preoperative 5-fluorouracil-based chemoradiotherapy followed by surgical resection.

Results. From December 2004 to April 2011, 70 LARC pts performed clinical staging with MR, EUS, and CT in a single institution. Patients characteristics were median age 71 years (range 46-85); males 48 (68.6%) and females 22 (31.4%); median distance from the anal verge 5.5 cm (range 0.5-12 cm). Clinical stages with MR were: 9 (12.8%) T2; 46 (65.8%) T3; 15 (21.4%) T4; 19 (27.1%) loco-regional node negative (N0) and 51 (72.9%) loco-regional node positive (N+). CT staging was discordant with MR staging in 17 (31.5%) pts for T and in 10 (16.6%) pts for N. EUS staging was discordant with MR staging in 16 (25.4%) pts for T and in 24 (38.7%) pts for N. The following table shows CT and EUS concordance with MR in relation to T and N stage.

Table - E9

	T2		T3		T4		N0		N+	
	CT vs MR	EUS vs MR	CT vs MR	EUS vs MR	CT vs MR	EUS vs MR	CT vs MR	EUS vs MR	CT vs MR	EUS vs MR
Concordance	4/6	4/8	23/35	35/44	10/13	8/11	15/16	17/19	35/44	22/44
	66.6%	50%	65.7%	79.5%	76.9%	72.7%	93.8%	89.5%	79.5%	50%
Discordance	2/6	4/8	12/35	9/44	3/13	3/11	1/16	2/19	9/44	22/44
	33.3%	50%	34.3%	20.4%	23.1%	27.3%	6.2%	10.5%	20.5%	50%

Discordance	T2	T3	T4	N0	N+
CT down-stage	0	7/12 (58.3%)	3/3 (100%)	0	9/9 (100%)
CT over-stage	2/2 (100%)	5/12 (41.6%)	0	1/1 (100%)	0
EUS down-stage	0	3/9 (33.3%)	3/3 (100%)	0	22/22 (100%)
EUS over-stage	4/4 (100%)	6/9 (66.6%)	0	2/2 (100%)	0

We found that 4/21 (19%) pts with pathological node positive (pN+) had at diagnosis negative N staging with MR; 6 (28.6%) pts had negative CT and 11 (52.4%) pts had negative EUS.

Conclusions. In this analysis major discordances with MR was in T staging for CT evaluation and in N staging for EUS. CT and particularly EUS showed a N down-staging compared to MR and pathological evaluation.

E10 THE PRESENCE OF NODAL METASTASES AND POOR OUTCOME IN ANAL CARCINOMAS ARE PREDICTED BY EXPRESSION OF YKL-40

Senetta R., Mistrangelo M.*, Cassenti A., Castellano I., Morino M.*, Milanesi E.**, Ricardi U.***, Chiusa L., Cassoni P.

*Department of Biomedical Sciences and Human Oncology, *Digestive and Colorectal Surgical Department and Centre of Minimal Invasive Surgery, **Oncological Centre for Gastrointestinal Neoplasms, ***Department of Radiotherapy, University of Turin, Molinette Hospital, Italy*

Background. Anal cancer incidence has increased considerably in recent years, especially among men aged under 45 years and HIV-positive patients. Anal cancer treatment has changed over the past two decades, shifting from radical surgery toward sphincter-conserving treatment based on radiotherapy (RT) and chemotherapy (CT). Conservative approach is highly effective, but treatment failures with relapses are still relatively common. Aim of the present study is to identify pathological/molecular markers effective in tracing a prognostic patient stratification, in order to optimize clinical/surgical therapeutic strategies. In a preliminary study on a small cohort of patients, we reported that YKL-40, a glycoprotein involved in radio-resistance in various solid tumours including squamous carcinomas of the head and neck region and gliomas, predicted poor outcome in anal cancer as well. Therefore, we analyzed the histopathological features of a series of 50 anal cancer biopsies prior to CT-RT and correlated histological and selected immunohistochemical parameters, including the radio-resistance marker YKL-40, with clinical outcome (overall survival [OS] and disease-free survival [DFS]).

Methods. Fifty biopsies of anal carcinomas were obtained from a consecutive cohort of patients between January 2003 and December 2010 at the University of Turin. Clinical and histopathological data were collected. Immunohistochemical analysis with antibodies raised against Ki67, p53, epidermal growth factor receptor (EGFR) and YKL-40 was performed. Statistical correlations among markers and clinical-pathological features and with clinical outcome were studied.

Results. All patients underwent synchronous CT-RT. Tumour recurrence after CT-RT treatment developed in 26% of patients and 8/50 patients died. A close correlation emerged between YKL-40 tumour expression (cytoplasmatic stain present in more than 20% of the neoplastic cells) and lymph node metastatic status ($p = 0.040$). Both these two variables, YKL-40 expression and node metastasis were significantly ($p < 0.005$) associated with shorter OS and DFS. Histological grade showed a significant correlation with DFS only ($p < 0.042$). HPV, HIV, tumour histological type, Ki67, p53 and EGFR expression were not related to OS and DFS.

Conclusions. Nodal metastases and YKL-40 expression proved to be the only significant prognostic markers of shorter survival in anal cancer, and to be directly correlated. Since YKL-40 expression in other solid tumours has been associated to a reduced response to RT, it could be suggested that YKL-40 positive anal carcinoma could benefit from a different therapeutic approach than RT and that in this subset of patients surgery could be considered as a first choice treatment.

E11 TREATMENT OF ADVANCED RECTAL CANCER WITH SYNCHRONOUS METASTASIS AT DIAGNOSIS: ANALYSIS OF 63 CONSECUTIVE CASES OF THE BOLOGNA MULTIDISCIPLINARY RECTAL CANCER GROUP

Di Fabio F.[1], Pinto C.[1], Pini S.[1], Di Tullio P.[1], Cuicchi D.[2], Iacopino B.[3], Lecce D.[2], Ugolini G.[2], Ercolani G.[4], Stella F.[5], Rojas Llimpe F.L.[1], Giaquinta S.[1], Martoni A.

[1]Medical Oncology Unit, [2]Surgery Unit, [3]Radiotherapy Unit, [4]Liver Surgery Unit, [5]Thorax Surgery Unit, S. Orsola-Malpighi Hospital, Bologna, Italy

Background. Twenty per cent of middle/low rectal cancer patients (pts) have synchronous distant metastasis (M1) at diagnosis. At present, the treatment strategy in this setting of pts is not defined. This monoinstitutional retrospective analysis evaluates treatment strategy and clinical outcome of three different pts groups.

Methods. Between January 2000 and April 2011 the Bologna Multisciplinary Rectal Group of S. Orsola-Malpighi Hospital evaluated 63 pts with rectal cancer M1 disease. Three different groups were defined: rectal cancer with resectable metastatic disease (group A); rectal cancer with potentially resectable metastatic disease (group B); and rectal cancer with unresectable metastatic disease (group C). Treatment strategy in different groups contemplated an individualized approach.

Results. The pts characteristics were: males 41 (65.1%), females 22 (34.9%); median age 61 years (35-83); median ECOG PS 0 (0-2); cT3 44 (69.8%), cT4 19 (30.2%); cN- 10 (15.9%), cN+ 53 (84.1%); M1 sites: liver 30 (47.6%), lung 8 (12.7%), liver and lung 11 (17.4%), ovary/peritoneal carcinosis 6 (9.5%), bone 2 (3.2%), 3 or more sites 6 (9.5%). Forty-one (65.1%) pts underwent surgery for primary rectal tumour, 28 (44.4%) pts for a first metastasis resection (22 liver, 2 lung, 1 liver + lung, 3 hysteroannexectomy), and 8 (12.7%) for a second metastasis resection (2 liver, 5 lung and 1 liver + lung). The distribution according to groups was: group A 10 (15.9%) patients, group B 23 (36.5%), and group C 30 (47.6%). Treatments for different groups are shown in the following table.

	Group A No. 10	Group B No. 23	Group C No. 30
Neoadiuvant chemoradiation	8	13	4
Conversion chemotherapy	1	6	1
Palliative chemotherapy	0	6	26
T surgery	9 (1 ongoing)	20	12
M surgery	7 (2 ongoing)	18 (1 ongoing)	3
T palliative treatment	1	1	18

Median overall survival (OS) of all the 63 patients was 27 months (95% CI 22-32). Median OS according to the three different groups was: group A 49 months, group B 32 months and group C 20 months. Patients submitted to metastasis resection

have higher median OS than those non resected, 32 months (95% CI 19-45) versus 16 (95% CI 8-24) (p = 0.003).

Conclusions. Treatment strategy in synchronous metastatic rectal cancer must consider possibility of distant metastasis resection. Long-term survival can be achieved using an integrated approach that includes conversion chemotherapy, neoadjuvant chemoradiotherapy and primary tumour and metastasis surgery.

E12 TOPICAL VITAMIN K1 IN THE MANAGEMENT OF SKIN RASH DURING ANTI-EGFR MONOCLONAL ANTIBODY TREATMENT IN PATIENTS WITH METASTATIC CANCER (ITALIAN OBSERVATIONAL STUDY)

Di Tullio P.[1], Barone C.[2], Pinto C.[1], Ferrari D.[3], Latiano T.[4], Orlandi A.[2], Di Fabio F.[1], Cassano A.[2], Rojas Llimpe F.L.[1], Pini S.[1], Amoroso A.[2], Maiello E.[4], Martoni A.[1]

[1]Medical Oncology Unit, S. Orsola-Malpighi Hospital, Bologna, Italy; [2]Medical Oncology Unit, Policlinico Gemelli, Rome, Italy; [3]Medical Oncology Unit, San Paolo Hospital, Milan, Italy; [4]Medical Oncology Unit, Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo (FG), Italy

Background. Cutaneous toxicity, and especially skin rash, is a predictable side-effect of anti-EGFR monoclonal antibody (mAb) therapy. Cutaneous toxicity can severely impact a patient's physical, psychological, and social well-being and can lead to discontinuations and treatment dose reductions. Preclinical studies have shown that vitamin K1 reactivated EGFR-mediated signal transduction after inhibition *via* EGFR receptor antagonists. The aim of this study was to evaluate the impact of vitamin K1 cream in skin rash management.

Methods. In four Italian Oncology Centers sequential pts at the first therapy with cetuximab/panitumumab for metastatic cancer were treated with vitamin K1 cream before the start of treatment (group A) or at the earliest onset of grade ≥2 skin rash (group B). General prophylactic measures were provided for all the patients before the start of anti-EGFR mAb treatment. Topical treatment with vitamin K1 (phytomenadione 0.1%) cream twice/die was performed both in group A and B continuously until the end of cetuximab/panitumumab treatment. Skin toxicity, according to NCI-CTC v3.0 grading system, was clinically evaluated every two weeks and in a standardized way, by taking pictures of 5 different body areas (face, fore/back-thorax, foot, right hand). Treatment benefit was evaluated according to symptom reduction and compliance with anti-EGFR mAb therapy.

Results. From February 2010 to March 2011, 70 pts (30 group A and 40 group B), 44M (62.8%) and 26F (37.2%), median age 63 years (range 28-82), were evaluated. The primary tumour site was 3 (4.3%) esophagus/stomach, 56 (79.9%) colon-rectum, 11 (15.8%) head-neck. Forty-eight (68.6%) pts were treated as first-line and 22 (31.4%) were pretreated. The regimen contained cetuximab in 58 (82.8%) pts and panitumumab in 12 (17.2%). The combination regimens were platinum-compounds-based in 31 (44.3%) pts, and irinotecan-based in 31 (44.3%); panitumumab was administered in monotherapy in 8 (11.4%) pts. The median time of vitamin K1 cream treatment in group A and B was 9 weeks (range 1-48) and 13 weeks (range 4-43) respectively; the oral semi-synthetic tetracycline therapy was associated in 17 (24.3%) pts. In group A all-grade skin rash was observed in 21 (70%) pts, grade 2 in 2 (6.6%) and grade 3 was detected in only 1 pt (3.4%). In group B a skin rash decrease to grade 0-1 was observed in 15 (37.5%) pts, 13 (32.5%) pts showed unchanged grade 2; the increase to grade 3 skin rash was observed in just 6 (15%) pts. At least one modification in cetuximab/panitumumab treatment was required in 1 (3.3%) pt of group A and 9 (22.5%) of group B.

Conclusions. Skin rash represents a good "marker" of efficacy in pts treated with anti-EGFR mAb. These preliminary results suggest a favorable impact of vitamin K1 cream in skin rash management, which should be considered in a future prophylactic clinical trial.

E13 TRIPLET CHEMOTHERAPY PLUS BEVACIZUMAB (FIR-B/FOX) ACCORDING TO *KRAS* GENOTYPE IN METASTATIC COLORECTAL CANCER (MCRC)

Bruera G.[1], Cannita K.[1], Di Giacomo D.[2], Lamy A.[3], Troncone G.[4], Marchetti A.[5], Coletti G.[6], Sabourin J.C.[7], Tosi M.[8], Ficorella C.[1], Ricevuto E.[1]

[1]Medical Oncology, S. Salvatore Hospital, University of L'Aquila, L'Aquila, Italy; [2]Department of Experimental Medicine, University of L'Aquila, L'Aquila, Italy; [3]Laboratory of Tumor Genetics, University Hospital, Rouen, France; [4]Department of Biomorphologic and functional sciences, University Federico II, Napoli, Italy; [5]Pathology, Civil Hospital, University G. D'Annunzio, Chieti, Italy; [6]Pathology, S. Salvatore Hospital, L'Aquila, Italy; [7]Department of Pathology, INSERM U614, Rouen University Hospital, Rouen, France; [8]INSERM U614, University of Rouen, Rouen, France

Background. FIr-B/FOx association, consisting of triplet chemotherapy (FIr/FOx) plus bevacizumab, may increase activity, efficacy and resection rate of liver metastases in MCRC patients (pts) (Bruera G, BMC Cancer, 2010). Bevacizumab-containing chemotherapy is active in *KRAS* wild-type (wt) and mutant (m) MCRC pts, even if ORR, PFS and OS seem to be lower in m pts (Hurwitz HI, Oncologist, 2009). Present data evaluates clinical outcome of FIr-B/FOx according to *KRAS* genotype.

Methods. Treatment schedule: weekly alternating bevacizumab (5 mg/kg days 1, 15)/irinotecan (160 mg/m^2) or oxaliplatin (80 mg/m^2) associated to weekly 5-fluorouracil (12h-timed-flat-infusion, 900 mg/m^2/d 1-2, 8-9, 15-16, 22-23); every 4 weeks. *KRAS* genotype was analyzed by SNaPshot (Di Fiore F, BJC, 2007) and/or direct sequencing for *KRAS* codon 12 and 13 mutations.

Results. Forty-five (90%) out of 50 pts enrolled in the FIr-B/FOx phase II study were evaluated at a median follow-up of 30 months. Twenty-five pts (56%) were *KRAS* wt, 20 (44%) *KRAS* m. Clinical features were balanced. Among the 25 *KRAS* wt pts at median follow-up of 33 months: ORR 88% (CI ± 14); median PFS 14 months (4-61+); median OS 38 months (8-61+). Liver metastasectomies (LM) were performed in 9 *KRAS* wt pts (36%): 56% of the 16 liver-MCRC pts; 80% of the 10 liver-only MCRC patients. Eighteen out of 25 *KRAS* wt pts were also *BRAF* wt: ORR 83% (CI ± 14); median PFS 13 months (4-44); median OS 31 months (8-58+). Among the 20 *KRAS* m pts at a median follow-up of 20.5 months: ORR 80% (CI ± 19); median PFS 12 months (3-52+); median OS 21 months (8-52+). LM were performed in 4 *KRAS* m pts (20%): 31% of the 13 liver-MCRC pts; 40% of the 10 liver-only MCRC pts.

Conclusions. Triplet chemotherapy plus bevacizumab (FIr-B/FOx association) may increase activity (ORR) and efficacy (PFS) in *KRAS* wt and, particularly, *KRAS* m MCRC pts; a trend toward a worse prognosis (OS) of *KRAS* m pts is confirmed.

E14 MICRORNA PROFILING AS PREDICTIVE FACTOR OF COMPLETE PATHOLOGICAL RESPONSE TO NEOADJUVANT CHEMO-RADIOTHERAPY IN PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER

Della Vittoria Scarpati G.[1], De Stefano A.[1], Falcetta F.[2], Carlomagno C.[1], Ubezio P.[2], Marchini S.[2], D'Incalci M.[2], De Placido S.[1], Pepe S.[3]

[1]Department of Molecular and Clinical Endocrinology and Oncology, University Federico II, Naples, Italy; [2]Laboratory of Cancer Pharmacology, Department of Oncology, "Mario Negri" Institute for Pharmacological Research, Milan, Italy; [3]Division of Oncology, University of Salerno, Italy

Background. MicroRNAs (miRNAs) are small, non-coding, RNA molecules involved in regulation of several cellular mechanisms. Specific miRNA have been found abnormally down-regulated or up-regulated in colorectal cancer and associated with prognosis or response to treatments. However, no study addressed their predictive role in rectal cancer. Therefore, we used microarray technology and RT-PCR to profile miRNA expression in patients (pts) affected by locally advanced rectal cancer, with the aim to identify a specific "signature" which correlates with pathological complete response to neoadjuvant chemo-radiotherapy.

Methods. Thirty-eight pts with locally advanced rectal cancer (uT3-4/N+) were treated with pre-operative capecitabine + oxaliplatin and pelvic conformal radiotherapy (45 cGy) followed by surgery (after 6-8 weeks). Pathologic response was scored according to the tumour regression grade (TRG) scale. MiRNA expression profile was analysed by microarray on fresh frozen biopsies, collected before treatment start, and confirmed by RT-PCR. The correlation between miRNA expression profile and the TRG, coded as TRG1 (pathologic Complete Response-pCR) versus TRG >1 (no pCR), was assessed by statistical analysis methods specifically designed for this study.

Results. Fourteen miRNAs were selected by arrays analysis as differentially expressed in TRG1 pts and 13 of them were confirmed by RT-PCR. In particular, 11 miRNAs (miR-1183, miR-483-5p, miR-622, miR-125a-3p, miR-1224-5p, miR-188-5p, miR-1471, miR-671-5p, miR-1909*, miR-630 and miR-765) were significantly up-regulated in TRG1 pts, while 2 miRNAs were down-expressed (miR-1274b and miR-720). miR-622 and miR-630 showed 100% sensitivity and specificity for TRG1 cases and were significantly correlated to EGFR ($\chi^2 = 11.793$; $p = 0.001$) and TS expression ($\chi^2 = 10.589$; $p = 0.001$).

Conclusions. A set of 13 miRNA is significantly correlated with pathologic complete response and might be considered a specific marker of response to pre-operative chemo-radiotherapy in locally advanced rectal cancer.

E15 MUCINOUS ADENOCARCINOMA HISTOLOGY (MA) PREDICTS REDUCED EFFICACY OF FOLFOX4 REGIMEN IN METASTATIC COLORECTAL CANCER (MCRC) COMPARED TO NON-MUCINOUS ADENOCARCINOMA (NMA). A RETROSPECTIVE ANALYSIS

Maisano R.*, Azzarello D.*, Maisano M.°, Nardi M.*

**U.O. Oncologia Medica, °U.O.C. Anatomia Patologica, A.O. "Bianchi-Melacrino-Morelli", Reggio Calabria, Italy*

MA is a histological subtype of colorectal cancer and accounts for 10-20% of the cases. Some studies have reported a poorer prognosis of MA compared to NMA in relation to younger age of the patients (pts), greater propensity for early spread to regional lymph nodes, more advanced stage at diagnosis and lesser response to chemotherapy. All pts with metastatic MA treated with FOLFOX4 as first-line chemotherapy were compared, in a retrospective analysis, with pts with metastatic NMA in the case-control ratio 1:2. From January 2002 to December 2009 we have treated 198 pts with FOLFOX4. Twenty-one (10.6%) had a histologically confirmed diagnosis of MA of CRC. The 42 control pts with NMA of MCRC were matched in random fashion. Patients characteristics of both groups were well balanced except for location of primary (right colon 35% in MA vs 20% in NMA, $p = 0.32$) and peritoneum (45% vs 25%, $p = 0.18$) and lymph nodes (25% vs 10%, $p = 0.23$) as sites of metastases. The primary endpoint was ORR, secondary endpoints were PFS and OS.

Results. About ORR we registered 15% of response in MA and 41.5% in NMA ($p = 0.073$). At the time of analysis (December 2010), after a median follow-up of 51 months, no pts with MA were alive compared to 5 pts with NMA. Median PFS was 4 months and 8 months for MA and NMA ($p = 0.001$) and median OS was 8 months vs 17.5 months ($p = 0.001$) respectively. Moreover only 8 pts (38%) out of 21 received 2nd-line chemotherapy in MA group compared to 31 (73%) out of 42 in NMA group ($p = 0.016$). In univariate and multivariate analysis histology (MA), PS (>1), CEA level (>5) and number of metastatic sites (>2) were found to be independent prognostic factors of poor response to chemotherapy. Although conflicting data on the association between mucinous histology and worse prognosis have been reported in literature, at least two recent retrospective studies (Negri FV et al., Ann Oncol, 16: 1305, 2005; Catalano V et al., Br J Cancer, 100: 881, 2009) are concordant with our results showing a lower efficacy of 5-fluorouracil based chemotherapy, even in combination with OXA or IRI, in the treatment of MA. Several genetic and biological features together with clinical factors may explain the different outcomes between MA and NMA but until now the scenario is confusing and more knowledge is necessary to optimize the treatment of this set of patients.

E16 PET-CT IN ANAL CANCER: OUR EXPERIENCE

Mistrangelo M., Pelosi E.*, Bellò M.**, Ricardi U.^, Milanesi E.^^, Cassoni P.§, Baccega M.°, Racca P.^^, Skanjeti A.**, Morino M.

*Digestive and Colorectal Surgery, Centre of Minimal Invasive Surgery, University of Turin, Molinette Hospital, Italy; *PET Center IRMET spa, Turin, Italy; **Department of Nuclear Medicine, ^Department of Radiotherapy, ^^Oncological Centre for Gastrointestinal Neoplasms, §Department of Biomedical Sciences and Human Oncology, University of Turin, Molinette Hospital, Italy; °Department of Nuclear Medicine, Molinette Hospital, Italy*

Purpose. Anal cancer is an uncommon malignancy of the gastrointestinal tract. Pre- and post-treatment staging of disease is often inaccurate, however. An emerging tool in noninvasive tumour staging is PET/CT, whose role in the clinical management of anal cancer is yet to be defined.

Methods and materials. At our Department, 53 consecutive patients diagnosed with anal cancer underwent PET/CT and computed tomography (CT) at pre-treatment workup, and then PET/CT and anal biopsy at 1 and 3 months follow-up after the end of treatment. Pre- and post-treatment PET/CT data sets were compared.

Results. At pre-treatment assessment, anal cancer was identified by PET/CT in 47 patients (88.7%) and by CT in 40 patients (75%). The detection rates rose to 97.9% with PET/CT and to 82.9% with CT (p = 0.042) when the 5 patients who had undergone surgery prior to this assessment and whose margins were positive at histological examination were censored. Perirectal and/or pelvic nodes were visualized by PET/CT in 14 patients (26.4%) and by CT in 7 (17.5%). Sentinel node biopsy was superior to both PET/CT and CT in detecting inguinal lymph nodes. PET/CT upstaged 39% of patients and downstaged 25%. Radiation fields were changed in 11% of patients. PET/CT at 3 months was more accurate than PET/CT at 1 month in evaluating outcomes after radiochemotherapy treatment: sensitivity was 100% vs 66.6%, and specificity was 97.4% vs 92.5%, respectively. The median follow-up was 20.3 months.

Conclusions. In this series, PET/CT detected the primary tumour more often than CT. Staging of perirectal/pelvic or inguinal lymph nodes was better with PET/CT; however, upstaging related to lymph node metastases might have been overestimated. Sentinel node biopsy was more accurate in staging inguinal lymph nodes. PET/CT should be performed at 3 months after the completion of treatment for assessing treatment efficacy.

E17 IMPACT OF PET SCAN IN DETECTING EXTRAEPATIC DISEASE IN POTENTIALLY RESECTABLE COLORECTAL CANCER LIVER METASTASIS PATIENTS

Rojas Llimpe F.L.[1], Di Fabio F.[1], Pinto C.[1], Pini S.[1], Di Tullio P.[1], Ercolani G.[2], Castellucci P.[3], Cappelli A.[4], Giampalma E.[4], Mutri V.[1], Martoni A.[1]

[1]Medical Oncology Unit, [2]Liver Surgery Unit, [3]Nuclear Medicine Unit, [4]Radiology Unit, S. Orsola-Malpighi Hospital, Bologna, Italy

Background. The aim of the Prometeo study was to define the specific diagnostic accuracy of different imaging techniques in patients with potentially resectable colorectal cancer liver metastasis. We focused this analysis on patients who did not undergo radical surgery because of extrahepatic disease.

Methods. In the 3-4 weeks prior to liver surgery, eighty-four consecutive patients with colorectal cancer liver metastasis referring to the Multidisciplinary Team of Sant'Orsola-Malpighi Hospital, Bologna, performed a computed tomography scan (CT), magnetic resonance (MR), 18F-FDG positron emission tomography (PET) and liver contrast-enhanced ultrasonography (CEUS1). Liver contrast-enhanced ultrasonography was also performed intra-operatively (CEUS2). All the imaging tests were performed according to the standard operative procedures.

Results. From December 2007 to August 2010, 58/84 patients enrolled in the Prometeo study performed CT and PET scan. In 11/58 (19.0%) patients the extrahepatic disease was detected by CT scan and/or PET scan or only by exploratory laparotomy. CT and PET scan equally detected extrahepatic disease in 6 (10.3%) patients: 2 abdominal lymph nodes, 1 bone metastasis, 1 abdominal lymph nodes/bone metastasis, 1 abdominal lymph nodes/lung metastasis and 1 lung/bone metastasis. In 3 (5.2%) cases bone metastases (1 patient) and peritoneal carcinomatosis (2 patients) were detected by PET scan despite CT negativity. In 2 (3.5%) patients peritoneal carcinomatosis was found at the time of surgery (CT and PET did not show extrahepatic disease).

Conclusion. The Prometeo study enrolled patients highly selected for potentially resectable colorectal cancer liver metastasis. In this patients setting the PET scan showed extrahepatic disease in 5.2% of cases.

E18 LAPAROSCOPIC OR OPEN RESECTION FOR METASTATIC COLORECTAL CANCER

Allaix M.E., Degiuli M., Mistrangelo M., Giraudo G., Marano A., Morino M.

Digestive and Oncological Surgery and Center for Minimally Invasive Surgery, University of Turin, Italy

Background. Few studies have investigated the surgical treatment of symptomatic metastatic colorectal cancer, and most of them reported results after open surgery. The aim of this study was to evaluate short-term and oncologic outcomes of laparoscopic resection (LR) for patients with stage IV colorectal cancer, compared to open resection (OR).

Methods. This study is a retrospective analysis of a prospective database. Only patients with a minimum follow-up of 12 months after LR or OR for metastatic colorectal cancer were included. All analyses were performed on an ''intention-to-treat'' basis.

Results. One hundred and sixty-two consecutive patients submitted to LR and 127 submitted to OR were included. No differences were observed in terms of demographic and clinical characteristics between the two groups. Conversion rate in LR group to OR was 26.5%, mostly because of locally advanced neoplasm (83.7%). A greater risk of conversion to laparotomy was noted among patients with a tumour size greater than 6 cm regardless the tumour localization (p = 0.08). Early postoperative course was significantly better for LR group, with a shorter hospital stay (p = 0.008), and similar postoperative complications (p = 0.853) and mortality rates (p = 0.958). LR for rectal cancer was associated with a higher morbidity compared to LR for colon cancer (p = 0.058). During a median follow-up of 72 months, there was no significant difference in overall survival between the two groups (p = 0.688).

Conclusions. Laparoscopic surgery for metastatic colorectal cancer is safe, without impairment of the overall survival. Further prospective and possibly randomized clinical trials are needed to confirm our suggestions.

E19 MAY GENETIC BACKGROUND AFFECT THE INCIDENCE RATES OF SOMATIC MUTATIONS IN *KRAS*, *BRAF*, AND *PIK3CA* GENES AMONG PATIENTS WITH COLORECTAL CARCINOMA? CLUES FROM SARDINIAN POPULATION

Palomba G.[1], Colombino M.[1], Olmeo N.[2], Massidda B.[3], Cuccu A.[2], Ionta M.T.[3], Contu M.[2], Capelli F.[4], Trova V.[5], Sedda T.[6], Farris A.[7], Tanda F.[8], Budroni M.[9], Sardinian Translational Oncology Group (STOG), Palmieri G.[1], Cossu A.[10]

[1]Istituto di Chimica Biomolecolare, CNR, Sassari; [2]Servizio Oncologia, ASL1, Sassari; [3]Oncologia Medica, Università di Cagliari; [4]Oncologia, ASL, Nuoro; [5]Oncologia, ASL, Alghero; [6]Oncologia, ASL, Oristano; [7]Oncologia Medica, Università di Sassari; [8]Anatomia Patologica, Università di Sassari; [9]Servizio Epidemiologia, ASL1, Sassari; [10]Istituto di Anatomia Patologica, AOU, Sassari, Italy

Background. In addition to *KRAS* mutations, it has been suggested that either *BRAF* or *PIK3CA* mutations might also confer tumour resistance to EGFR-targeted antibodies in colorectal cancer (CRC). However, conflicting data are being generated regarding the prevalence of *BRAF* and *PIK3CA* mutations in different populations.

Methods. From April 2009, tissue sections from CRC patients (n = 436) with ascertained Sardinian origin were prospectively collected. Genomic DNA was isolated and screened for mutations in *KRAS*, *BRAF*, and *PIK3CA* genes by automated DNA sequencing.

Results. *KRAS* tumour mutation rate was 30% (130/436 positive cases), with no significant differences according to sex and age. However, distribution of positive cases was different across the island [75/186 (40%) in North Sardinia vs 55/250 (22%) in Middle-South Sardinia]. Since this is consistent with the discrepancy in distribution of germline mutations for other malignancies (breast cancer and melanoma, as we previously described) within Sardinian population, one could speculate that a different genetic background may influence the frequency of *KRAS* somatic mutations. Among 384 CRC patients, whose somatic DNA was available for further analyses, we detected only 1 case (0.3%) with mutated *BRAF* gene (V600E). Conversely, *PIK3CA* was found mutated in 164/384 (43%) patients, again with no significant differences according to sex and age. For this gene, an inverse distribution of the mutation prevalence was observed within Sardinian population [69 (38%) in 180 cases from northern vs 95 (47%) in 204 cases from central-southern island]. In our series, *PIK3CA* mutations has no role in predicting response to anti-EGFR antibodies in patients with wild-type *KRAS*.

Conclusions. These findings further support the hypothesis that patients' origin and genetic background may contribute to determine the incidence rate of somatic mutations in cancer genes.

E20 BIOMOLECULAR, BIOCHEMICAL, RADIOLOGIC EVALUATION AND SAFETY OF CHEMOTHERAPY WITH BEVACIZUMAB IN TREATMENT OF PATIENTS AFFECTED BY mCRC

Rossi L.[1], Veltri E.[2], Colonna M.[2], Zoratto F.[1], Vari S.[1], Mottolese M.[3], Di Seri M.[4], Romiti A.[5], Longo F.[4], Giannarelli D.[6], Barucca V.[5], Zullo A.[7], Tomao S.[1]

[1]Department of Medical-Surgical Science and Biothecnology, Oncology Unit, S. Maria Goretti Hospital, Latina, Sapienza University of Rome; [2]Oncology Center Ettore MS Conti, Luigi di Liegro Hospital, Gaeta; [3]Department of Pathology, Regina Elena National Cancer Institute, Rome; [4]Department of Experimental Medicine, Policlinico Umberto I, Sapienza University of Rome; [5]Medical Oncology, S. Andrea Hospital, Sapienza University of Rome; [6]Biostatistics Unit, Regina Elena National Cancer Institute, Rome; [7]Gastroenterology and Digestive Endoscopy, Nuovo Regina Margherita Hospital, Rome

Background. A retrospective analysis on patients affected by mCRC was performed to assess bevacizumab clinical benefit according to KRAS mutational status and metastatic sites, correlation between MKS values and clinical response and tolerability to treatment.

Methods. 121 patients received Folfiri or FolFoX plus bevacizumab in first-line chemotherapy. Before therapy, patients were investigated with CT scan and MKS, that were repeated after 3 and 2 months of chemotherapy respectively. KRAS mutation was investigated in 108 patients. Chi-square test and logistic regression analysis were used to determine statistical significance.

Results. Overall RR of 42% and CB of 83% were obtained, with correlation between MKS and clinical response of 87%. 51% of sample presented only hepatic metastases while 48% showed multiple metastatic sites: RR was 50% in hepatic metastases group vs 34% multiple metastatic sites (HR 1.90; 95% CI 0.91-3.96; p = 0.08); CB was 90% vs 76% respectively (HR 2.97; 95% CI 1.05-8.36; p = 0.03). 64% patients were wild-type, remaining 36% were mutated: RR was 49% in *wt* group vs 34% *mut* group (HR 0.51; 95% CI 0.23-1.16; p = 0.11); CB was 87% *wt* vs 82% *mut* (HR 0.69; 95 CI 0.23-2.01; p = 0.49). Correlation between MKS and clinical response was 84% *wt* vs 94% *mut*. Among factors that influence the response to bevacizumab, only the change in markers was significantly correlated with RRs (p = 0.05) and CB (p <0.0001). 69% of overall experienced any grade toxicities. Most common G3-G4 toxicities were neutropenia 14%, diarrhea 4% and vomiting 2%. G1-G2 bevacizumab toxicities were bleeding 13%, hypertension 11%, DVT 7%, proteinuria 2% and pulmonary embolism 1%; no G3-G4 bevacizumab toxicities were showed.

Conclusion. Bevacizumab provided an advantage in terms of RR, not statistical significant, in KRAS *wt* group, also induced important RR and CB after short time of treatment with a statistically significant correlation between variation of MKS values, RRs and CB. Finally, bevacizumab provided statistical significance CB in hepatic metastases group and it was well tolerated.

E21 MICRO-COUNT®: A NEW METHOD OF IMMUNOLABELING CAPTURE WITH DIRECT COUNTING AND SEPARATION OF CIRCULATING TUMOUR CELLS

Torchio M.[1], Danova M.[1], Mazzini G.[2]

[1]S.C. Medicina Interna e Oncologia Medica, Ospedale di Vigevano, A.O. di Pavia,; [2]Istituto di Genetica Molecolare IGM-CNR, Pavia

Background. Circulating tumour cells (CTCs) may provide new insights in clinical oncology aiming toward individualized therapy. The biological characterization of these cells will furnish additional important information. In this field, technical-methodological approaches are crucial and there is a great need for development of sensitive technologies able to avoid stress on the cells during manipulation, to preserve cell viability and proliferation capability. The cost of such methods is another issue that should be addressed.

Materials and methods. We describe a system developed in our laboratory and recently patented (MICRO-COUNT®), that exploits the immunolabelling capture with the peculiar advantages of conventional microscopy in samples containing extremely rare cells. Our system is based on a simple, low-cost procedure, capable of an efficient and selective separation of CTCs from whole blood, without pre-labelling or processing samples. We focused on EpCAM +ve, cytokeratins +ve and CD45 –ve cells. The second labelling step is performed using Dynal magnetic beeds directly visible by light microscopy. A panel of colorectal cancer cell lines was used in spiking experiments: SNU-C2B and SW-480, with different levels of EGFR expression; HCT116 and COLO-320 with different levels of CD40 expression.

Results. We successfully identified viable colorectal cancer cells diluted in the peripheral blood with a range of 2-5 CTCs per mL and approximately 55% purity. The innovative step of MICRO-COUNT® is the possibility to perform the entire procedure in a multiwells plate directly monitoring each labelling step. This is allowed by a dedicated magnetic plate fitting the shape of the disposable standard 8 multiwells plate. Isolated cells can be directly counted in phase contrast unlabelled, rapidly tested for their viability, further characterized after labelling with different surface markers and transferred to a vial for molecular biology studies.

Conclusions. Our system allows a rapid and accurate identification/collection of viable CTCs. It makes possible further analyses such as studies on EGFR expression and on CD40/sCD40L pathway in colorectal cancer.

E22 TRAP1 INDUCES A MULTI-DRUG RESISTANT PHENOTYPE IN BRAF V600E COLORECTAL CARCINOMA CELLS BY REDUCING THE ACTIVATION OF MITOCHONDRIAL ERK AND FAVORING RESISTANCE TO APOPTOSIS

Landriscina M.[1], Maddalena F.[1], Piscazzi A.[1], Costantino E.[1], Laudiero G.[2], Lombardi V.[1], Natalicchio M.I.[3], Antonetti R.[3], Fersini A.[4], Matassa D.S.[2], Esposito F.[2]

[1]Sezione di Oncologia Medica, Dipartimento di Scienze Mediche e del Lavoro, Università degli Studi, Foggia; [2]Dipartimento di Biochimica e Biotecnologie Mediche, Università degli Studi Federico II, Napoli; [3]Laboratorio di Biologia Molecolare, Azienda Ospedaliero-Universitaria Ospedali Riuniti, Foggia; [4]Sezione di Chirurgia Generale, Dipartimento di Scienze Chirurgiche, Università degli Studi, Foggia

Human colorectal carcinomas (CRCs) harboring the BRAF V600E mutation are poorly responsive to chemotherapy. Our group has previously reported that TRAP1, a mitochondrial chaperone with antiapoptotic function, is involved in multi-drug resistance in human CRC cells and is up-regulated in the majority of human CRCs. Since TRAP1 is a member of a cytoprotective mitochondrial network selectively active in tumours responsible for antagonizing the proapoptotic activity of cyclophilin D and the opening of the mitochondria transition pore, and since the activation of mitochondrial ERK protects cancer cells from death through inhibition of the permeability transition, we evaluated whether the drug-resistant phenotype of human BRAF-mutated CRCs depends on the activation of TRAP1 pathway. We analyzed the role of TRAP1 in favoring drug-resistance and the activation of mitochondrial ERK in BRAF V600E HT-29 CRC cells compared to KRAS G13D HCT-116 CRC cells and BRAF/KRAS wild type Caco-2 CRC cells. BRAF-mutated CRC cells revealed a reduced sensitivity to oxaliplatin- and irinotecan-induced apoptosis compared to BRAF-wild type CRC cells and this correlated with increased levels of activated mitochondrial ERK. Of note, the selective down-regulation of TRAP1 expression by si/shRNAs resulted in reduced levels of pERK in mitochondria, suggesting a role of TRAP1 in the activation of mitochondrial ERK in human CRC cells. Furthermore, the activation of ERK pathway by EGF in CRC cells resulted in the transcriptional up-regulation of TRAP1 expression and this activation was inhibited by the selective inhibition of MEK. Consistently, human BRAF/KRAS-mutated CRCs exhibited increased protein levels of TRAP1. Finally, the selective inhibition of TRAP1 expression resulted in the re-sensitization of HT-29 CRC cells to antiblastic agents. These evidences suggest that TRAP1 expression may be regulated by EGF in CRC cells and that the drug-resistant phenotype of human BRAF-mutated CRCs may depend on the selective activation of mitochondrial ERK through TRAP1 and the resulting inhibition of the permeability transition. Thus, TRAP1 inhibition may be regarded as a novel therapeutic strategy in BRAF-mutated human CRCs.

E23 BRAF MUTATION IN METASTATIC COLORECTAL CANCER: RELATION WITH EGFR-TARGET THERAPY CETUXIMAB AND PANITUMUMAB

Bertona E., Forti L., Negru M.E., Rigon E., Genestroni S., D'Agostino F., Galetto A., Saggia C., Rossi V., Gaudino E., Alabiso O.

S.C. Oncologia, A.O.U. Maggiore della Carità di Novara

Background. KRAS mutations occur in 35-45% of metastatic colorectal cancers (mCRC) and affect the efficacy of EGFR-targeted therapy and the survival of mCRC patients. Aim of this study is to investigate new predictive or prognostic molecular markers of resistance.

Materials and methods. We retrospectively analyzed objective tumour response, time to progression (TTP) and overall survival (OS) in relation to V600E mutation of BRAF gene in 37 cetuximab or panitumumab treated KRAS wild-type mCRC patients (4 patients received panitumumab, 17 cetuximab + irinotecan + fluorouracil, 10 cetuximab + oxaliplatin + fluorouracil and 6 cetuximab + irinotecan).

Principal findings. According to RECIST criteria, patients were classified into two groups: 23 responsive patients (R, SD+RP: 62.16%) and 14 non-responsive patients (NR, PD: 37.84%). 3/37 (8.10%) had BRAF mutation. All R patients were BRAF wild-type, while BRAF mutations belonged to NR patients. The whole population had a mean TTP of 280 days and a mean OS of 1225 days. For KRAS and BRAF wild-type group, mean TTP and OS were respectively 295 and 1295 days. Different survivals were observed amongst R and NR patients (Table 1). Within the NR group, BRAF mutated patients had lower survival (Table 2).

Conclusions. According to the literature, in this study BRAF mutations are associated with worse survival in mCRC patients, suggesting a prognostic role of this marker. It's also to be determined its predictive meaning for anti-EGFR therapies response.

Table 1

	mean TTP	mean OS
R patients	348	1481
NR patients	167	803

Table 2

NR patients	mean TTP	mean OS
BRAF wild-type	183	905
BRAF mutation	110	432

E24 PRESENCE OF APOPTOSIS IN DIAGNOSTIC BIOPSIES PREDICTS COMPLETE RESPONSE (TRG1) FOLLOWING PREOPERATIVE CHEMO-RADIOTHERAPY IN RECTAL CANCER

Senetta R., Mistrangelo M.*, Racca P.**, Spadi R.**, Chiusa L., Morino M.*, Munoz F.H.***, Ricardi U.***, Sandrucci S.*, Cassoni P.

*Department of Biomedical Sciences and Human Oncology, Molinette Hospital, University of Turin, Italy; *Digestive and Coloproctological Surgical Department and Centre of Minimally Invasive Surgery, University of Turin, Italy; **ColoRectal Cancer Unit, Medical Oncology 1, Hematology and Oncology Department, A.O.U. San Giovanni Battista, Turin; ***Department of Radiotherapy, University of Turin*

Background. Preoperative chemo-radiotherapy (CT-RT) has been used as a major treatment modality to improve local control and survival in rectal cancer. Response to CT-RT robustly differs among individual tumours. In the present study, we searched for histological/immunohistochemical predictive indicators and correlated them with evaluation of tumour regression grade (TRG) adapted from Mandard.

Methods. Twenty-nine rectal cancer patients who underwent preoperative CT-RT were studied between January 2006 and December 2010. Biopsy specimens were obtained from rectal cancer before preoperative CT-RT. Response to CT-RT was determined by histopathologic examination of resected specimens and classified as complete response (TRG1) or partial/absent response (TRG 2-5). On biopsies we studied tumour grade, number of mitosis/3HPF, inflammatory infiltrate, presence of apoptosis and desmoplasia. Immunohistochemical analysis with antibodies raised against caveolin-1 and YKL-40 was performed. Pathological features and immunohistochemistry results on the biopsies were correlated to TRG of the surgical specimens.

Results. None of pathological parameters proved predictive of complete CT-RT response, except apoptosis. The presence of apoptosis on the biopsy specimens proved to significantly correlate to complete response ($p = 0.043$, χ^2: 2.978). In detail, 83% of partial or non-responders had no apoptosis on the biopsies while 67% of patients with conspicuous apoptosis on the diagnostic biopsy were complete responders. On a preliminary subset of patients, absence of YKL-40 staining on biopsies proved to be correlated with complete response as well.

Conclusions. Apoptosis-inducing genes seem to play a key role in predicting response to RT. As previous reported genes promoting apoptosis showed higher expression in complete response to RT whereas apoptosis inhibitors showed higher expression in non-responders. Our results confirm and apply these previous molecular data to histology. The absence of YKL-40 staining seems to be related to TRG1. In spite of the small number of cases, the concurrent study of both histological and immunohistochemical parameters could be used on biopsy specimens to predict CT-RT tumour response and, in future, to personalize the therapeutic approach.

E25 MicroRNA/mRNA GENE EXPRESSION PROFILE IN COLORECTAL CANCER PATIENTS

Piepoli A., Panza A., Latiano T.[1], Gentile A., Biscaglia G., Copetti M.[2], Tavano F.[3], Palumbo O.[4], Lombardi L.[1], Mastrodonato N.[3], Carella M.[4], Di Sebastiano P.[3], Pellegrini F.[2], Maiello E.[1], Andriulli A.

Department of Gastroenterology, [1]Department of Oncology, [2]Bio-Statistics Unit, [3]Department of Surgery, [4]Medical Genetic Unit, IRCCS "Casa Sollievo della Sofferenza", San Giovanni Rotondo (FG), Italy

Background and aim. miRNAs are 19-25 nucleotide long, non protein-coding RNA molecules that regulate the expression of a wide variety of genes, including some involved in cancer development. This regulation is often achieved by reducing the stability of target mRNA molecules. The aim of this study was to profile the expression of miRNAs in colorectal cancers (compared with that in the normal mucosa) and to predict their putative target transcripts by the combined analysis of mRNA expression levels in the same tissues.

Method. We evaluated miRNAs and mRNAs expression levels in 19 colorectal cancers and adjacent, normal mucosa by using Affymetrix GeneChip, miRNA Array (7815 probe sets) and Human Exon Array 1.0 ST (22,011 annotated genes), respectively. Normalization of miRNA and mRNA array datasets were performed by Robust Multi-array Average (RMA) procedure using the Partek Genomic Suite software. A random forest procedure for regression analysis was followed, using "R" statistical software, to predict miRNA-mRNA interactions: the mean decrease in accuracy allowed us to select the candidate miRNA to be associated to each target mRNA.

Results. 50 miRNAs and 568 mRNAs whose expression was significantly altered in cancers ($p < 0.01$ and $p < 5 \times 10^{-5}$ respectively, with a FDR of 0.05 and fold change less than -2 or greater than 2) were selected after data normalization. Based on the random forest analysis we could identify a small number of candidate miRNAs whose increased expression in neoplastic tissues was significantly correlated with a decreased expression of target mRNA. These negative correlations were also observed in *in silico* analysis (MicroCosm, Target Scan and PicTar) confirming that our identified transcripts might be indeed targets of miRNA-driven degradation.

Conclusion. Our combined analysis of miRNA and mRNA expression level changes in colorectal cancer tissues allowed us to identify putative target transcripts of specific miRNA. Some of these evidence is currently the subject of intensive investigation in our laboratory.

E26 AVASTIN® IN THE TREATMENT OF SEQUENTIAL CHEMOTHERAPY AND SURGERY IN LIVER METASTASES FROM COLORECTAL CANCER

Chiarenza M., Dimarco R., Sciacca D., Mazzola A., Aiello R.A., Alì M., Bagnato S., Di Leo M.G., Fallica G., Scandurra G., Taibi E., Mongiovì S.*, Caruso M.

*Humanitas Centro Catanese di Oncologia (CCO), Department of Medical Oncology, *Department of Surgical Oncology, Catania, Italy*

About 20% of patients (pts) with colorectal cancer show liver metastases (mts) at diagnosis while about 50% develop within 5 years. Several clinical studies have long demonstrated the efficacy of adjuvant chemotherapy (CT) after surgical resection of liver metastases. The combination of 5-FU/capecitabine with OXA/CPT-11 seems to be more effective than monotherapy with fluorouropirimidine while the use of Avastin® in adjuvant setting is still under investigation and cannot be taken as a standard treatment. Forty pts affected by colorectal cancer with liver mts,

18 F, 22 M were treated. Fifteen have been treated with CT + Avastin, 25 only with CT. All pts underwent radical surgery on the liver. The responders to neoadjuvant treatment were further treated with additional cycles of adjuvant CT, in total 12 cycles. No patient has performed maintenance therapy with Avastin. Patients who were treated with Avastin + CT have made a number of cycles before arriving at the surgery between 4 and 6 cycles, while those who have played only CT have just cashed a number of cycles between 6 and 12. The pre-treatment with CT has given RP (45%), SD (24%), PD (32%); pre-treatment with Avastin plus CT gave RP (87%), SD (13%), no PD. The surgery was radical in all patients. At follow-up pts who carried only CT, 40% reported PD liver, lung 50% PD and 10% on other sites. Patients who carried Avastin + CT, 70% maintained a CR, only 8% had PD of liver, 22% had PD at other sites. Our experience has demonstrated the efficacy of a combination of CT and Avastin in the preoperative phase of pts with the most of liver metastases. Treatment with Avastin received a greater response on liver mts allowing radical surgery without increasing the budget of postoperative complications. Patients who carried Avastin plus CT have prompted a number of cycles for the less radical surgery. Moreover, the number of PD hepatic impairment and time to relapse were lower than in pts treated with CT alone.

E27 CEA AND CA19.9 AS EARLY PREDICTORS OF PROGRESSION IN ADVANCED/METASTATIC COLORECTAL CANCER PATIENTS RECEIVING OXALIPLATIN-BASED CHEMOTHERAPY AND BEVACIZUMAB

Licchetta A., Roviello G., Pascucci A., Conca R., Chiriacò G., Petrioli R., Francini G.

Section of Clinical Medical Oncology, University of Siena

Background. A relatively recent approach to metastatic colorectal (CRC) disease has focused on oxaliplatin (l-HOP)-based chemotherapy combined with the new antiangiogenic agent bevacizumab (Bev). The aim of this study was to evaluate the changes of the tumour markers CEA and CA19.9 as early predictors of progression in advanced/metastatic CRC patients receiving l-HOP-based chemotherapy and Bev.

Methods. Serum CEA and CA19.9 levels were measured prior to chemotherapy and every 4 weeks after initiation of targeted therapy. All first rises in CEA and CA19.9 during chemotherapy were correlated with response to treatment as determined by conventional ig techniques.

Results. Sixty-nine patients (79.3%) of 87 with complete marker monitoring had initially increased CEA readings, and 56 (64.3%) had initially increased CA19.9 readings. By ROC analyses, the areas under the curves were 0.83 (95% CI 0.73-0.91) for variable CEA cut-off values and 0.80 (95% CI 0.67-0.89) for variable CA19.9 cut-off values, respectively, for distinguishing progression versus remission or stable disease. The use of combined tumour markers suggested that a concomitant increase ≥25% of CEA and CA19.9 distinguished a PD from NC/PR/CR with 84.8% sensitivity, 98.6% specificity, a positive predictive value of 93.3% and a negative predictive value of 96.6%. A greater than 25% reduction in CEA or Ca19.9 levels exhibited a positive predictive value for response to treatment of 96.6% and 90.1%, respectively. A ≥50% reduction in CEA or CA19.9 levels during treatment showed to be a prognostic factors for a better PFS ($p = 0.002$ and $p = 0.009$, respectively).

Conclusion. Repeated measurements of CEA and CA19.9 in metastatic CRC patients are useful in monitoring response to the new treatment approach consisting of l-HOP-based chemotherapy and Bev. Rises in these tumour markers may early signal the need to change chemotherapy because of the occurrence of progression as then confirmed by imaging procedures.

E28 IMPACT OF TARGETED THERAPY IN NEOADJUVANT TREATMENT OF COLORECTAL CANCER RESECTABLE LIVER METASTASES

Quaranta A., Cursio O.E., Di Lascio S., Amoruso A., Strippoli A., Orlandi A., Quirino M., Basso M., Schinzari G., Cassano A., Barone C.

Division of Medical Oncology, Università Cattolica del Sacro Cuore, Roma

Background. This study was performed retrospectively to assess if the addition of cetuximab or bevacizumab to irinotecan/oxaliplatin, 5-fluorouracil (5-FU), leucovorin (FA), administered as neoadjuvant chemotherapy, is associated with improved disease-free survival (DFS) and overall survival (OS) in patients with initially resectable colorectal liver metastases (CRM).

Patients and methods. Fifty-four patients with CRM that underwent hepatic resection during 2003 to 2005 were included. Group 1 (n = 27) patients received neoadjuvant FOLFOX/FOLFIRI and Group 2 (n = 27) FOLFOX/FOLFIRI plus cetuximab or bevacizumab.

Results. The objective response rate to chemotherapy was 92.6% (n = 50), with disease stabilization in 10 patients (18.5%). Treatment was well tolerated and all patients underwent a liver resection R0 following chemotherapy. After a median follow-up of 26 months, median survival for all patients was not reached. Median time to relapse was 12 months in all patients. There was no significant difference in OS and DFS between the two treatment groups (HR 1.10; 95% CI 0.30-4.14; $p = 0.85$ and HR 1.73; 95% CI 0.87-3.95; $p = 0.10$, respectively).

Conclusions. These data suggest that in patients with initially resectable CRM the addition of targeted agents to traditional cytotoxic neoadjuvant regimens is not associated with significant increase in OS or DFS.

E29 CLINICAL AND GENETIC CHARACTERIZATION OF DIHYDROPYRIMIDINE DEHYDROGENASE (DPD) DEFICIENCY IN FLUOROPYRIMIDINE-TREATED PATIENTS CARRYING THE DPYD*2A ALLELE

Del Re M.[1], Barbara C.[2], Loupakis F.[3], Butera A.[4], Zampino M.G.[5], Rondini M.[6], Aschele C.[6], Celio L.[7], Michelucci A.[8], Simi P.[8], Bocci G.[1], Di Paolo A.[1], Masi G.[3], Falcone A.[3], Cappuzzo F.[2], Danesi R.[1]

[1]Division of Pharmacology, Department of Internal Medicine, University of Pisa; [2]Division of Medical Oncology, Azienda USL 6, Livorno; [3]Division of Medical Oncology, Department of Oncology, Transplants and New Technologies in Medicine, University of Pisa; [4]Division of Medical Oncology, AORN Garibaldi, Catania; [5]Department of Medicine, European Institute of Oncology, Milano; [6]Department of Medical Oncology, E.O. Ospedali Galliera, Genova; [7]Medical Oncology Unit 2, National Cancer Institute, Milano; [8]Cytogenetics and Molecular Genetic Unit, University Hospital, Pisa, Italy

Background. The therapeutic efficacy and toxicity of fluoropyrimidines are, at least in part, related to the balance between anabolism of the drug to its nucleotides, which inhibit thymidylate synthase and are incorporated into RNA and DNA, and the catabolic pathway dependent on dihydropyrimidine dehydrogenase (DPD), which is the initial and rate-limiting step in pyrimidine degradation. Over the last decade, it has become clear that DPD regulates the amount of 5-FU available for anabolism thereby affecting its pharmacokinetics, toxicity, and efficacy. Moreover, an uncommon variant of the DPD gene, consisting of a G to A mutation in the splicing recognition sequence of intron 14 (IVS14+1G >A) of the DPD-encoding gene (DPYD*2A), produces a non-functional enzyme due to skipping of exon 14 and is potentially associated with life-threatening toxicity.

Aim. This study provides a description of the clinical features of fluoropyrimidine-induced toxicity in patients homo- or heterozygous for DPYD*2A.

Patients and methods. Six patients given FOLFOX, capecitabine or 5-FU test dose (425 mg/m^2) were genotyped. They suffered from the following toxicities (WHO criteria): diarrhea and febrile neutropenia grade 3-4, nausea-vomiting, stomatitis, piastrinopenia, alopecia, hand-foot syndrome grade 3 and anemia grade 2. Blood samples for DNA analysis were collected and used to screen patients for DPD polymorphisms by PCR and automatic sequencing of the entire coding region.

Results. Five patients were found heterozygous IVS14+1GA (DPYD*1/*2A) and one patient was homozygous mutant IVS14 + 1AA (DPYD*2A/*2A). The homozygous patient was initially tested with a reduced 5-FU test dose and showed diarrhea grade 2, mucositis grade 3, anemia grade 1, piastrinopenia grade 3, febrile neutropenia grade 4, complete alopecia and *Staphylococcus aureus* sepsis. This patient required 20 days of hospitalization and was managed with antibiotics, platelet transfusion, port removal, G-CSF administration and parenteral nutrition.

Conclusions. Although the frequence of DPYD*2A allele is low, the screening for DPD mutation is clinically relevant to avoid the severe toxicities or death in patients treated with fluoropyrimidine-containing regimens.

E30 CLINICAL OUTCOME IN ELDERLY PATIENTS WITH COLORECTAL CANCER: A SINGLE CENTER EXPERIENCE

Licitra S., Torazzo R., Posca T., Manachino D., De Marino E.

Oncologia Medica, Ospedale S. Andrea, Vercelli

Background. Clinical trials suggest a survival benefit of chemotherapy in elderly patients (pts) with colorectal cancer. However tolerability is still uncertain and often this population doesn't receive treatment in right place.

Methods. We assessed chemotherapy use, tolerability and survival outcomes in a retrospective analysis of colorectal cases in the over 70 age group of unselected pts in our hospital.

Results. Fifty-three pts received chemotherapy, between 2008 and 2010, mean age 75 (range 70-87), 29 males and 24 females; 52 had primary tumour resected, 4 metastasectomy. Twenty-seven pts had hypertension, 12 diabetes, 6 cardiopathy, 3 neurologic disease, 14 had lower comorbidities. ECOG Performance Status (PS) was 0 (22%) in 12/53, 1 (52%) in 28/53, 2 (24%) in 13/53. In our series 15/16 (93%) with stage III were appropriate for intensive (XELOX, FOLFOX4) adjuvant therapy and in stage IV were appropriate for intensive therapy 23/37 (62%) as initial therapy, 15/29 (51%) in first progression 4/12 (33%) after second progression, 4/12 (33%) pts received more than 3 lines of chemotherapy. Bevacizumab was added to 16 pts; cetuximab to 6 pts. The remainder received only a single drug. Fifteen pts started 20% reduction dose because of age, comorbidity, PS. There were no chemotherapy related deaths. In adjuvant group only one patient required hospital admission because of gastrointestinal toxicity G4 and delayed treatment. Only one patient discontinued chemotherapy, 15 (90%) pts completed treatment and received >90% of the planned dose. Sixteen pts are living without cancer after a median follow-up of 18 months. In metastatic group 21 (56%) pts required hospital admission and delayed chemotherapy because of major toxicities: 24% neutropenia G4; 0.02% anemia G3; 45% diarrhea G3-G4; 13% skin toxicity G3; 0.02% neurosensory G3, 0.02% allergic reaction (oxaliplatin). Sixteen (50%) pts are living with metastatic disease.

Conclusions. Intensive regimen of chemotherapy in elderly with colorectal cancer appears a well tolerated and manageable approach. Tolerability seems related to performance status, multiple comorbidity and biological age.

E31 MITOMYCIN C AND RALTITREXED IN ADVANCED COLON-RECTAL CANCER (mCRC) PATIENTS: PRELIMINARY RESULTS

Belloni P., Cozzi C., Toniolo D., Zannier F., Candido P., Della Torre S., Vismara A., Faricciotti A., Corradini M., Bollina R.

Oncology and Hematology Departement, A.O. G. Salvini, Rho (Milan)

Background. Sequential combinations of 5FU and irinotecan or oxaliplatin with bevacizumab or cetuximab are currently used as 1st, 2nd and 3rd line therapy for MCRC. Multiple trials are also investigating the concomitant use of this drugs up-front. Progressing pts with an acceptable PS often continue to require treatment. Mitomycin C and raltitrexed have shown clinical activity in adenocarcinomas of multiple sites and have a favourable toxicity profile.

Methods. This study was designed to explore the safety and efficacy of mitomycin C+ raltitrexed in pts with MCRC who previously failed therapy with a fluoropyrimidine and irinotecan or oxaliplatin or both and bevacizumab or cetuximab or both.

Regimen: mitomycin C 6 mg/m^2 day 1 every four weeks and raltitrexed 1 mg/m^2 day 1, 8 and 15 every four weeks.

Eligibility criteria included MCRC after failure of at least two lines of chemotherapy or with important heart comorbidity, age 18-80 yrs, ECOG-PS 0-3, adequate organ function, measurable disease, assigned informed consent.

Primary endpoints were toxicity, clinical benefit and response rate; overall survival as secondary endpoint.

Treatment courses were repeated every 4 weeks until progressive disease, unacceptable toxicity or patient refusal occurred.

Results. From September 2009, 57 cycles of chemotherapy were administered. Fifteen out of 17 pts are evaluable for response according to RECIST criteria. There were 0 complete response (CR), 3 (20%) partial response (PR) for an overall response rate of 20% and 2 (14%) stable disease (SD). Disease

control rate 34%. Patients responders are one in second-line chemotherapy and two in third-line chemotherapy.

Seventeen pts are evaluable for toxicity according to the NCI criteria. No grade 3-4 toxicities were observed. Liver toxicity grade 1-2 in 9 pts (53%), diarrhoea grade 2 in 2 pts (12%) and thrombocytopenia grade 1 in 1 pt (6%). No life threatening event occurred.

Conclusions. Preliminary data suggest that this schedule is well tolerated and may abrogate disease progression in approximately 30% of the pts refractory to 5FU, irinotecan, oxaliplatin, bevacizumab and cetuximab. The study is ongoing.

E32 FEASIBILITY OF TRIPLETS (5-FU, OXALIPLATIN AND IRINOTECAN BASED) IN FRONT AND SUBSEQUENT LINES OF METASTATIC COLORECTAL CANCER PATIENTS

Longobardi C.[1], Brandi G.[1], Bruera G.[2], Corbelli J.[1], De Rosa F.[1], Di Girolamo S.[1], Casolino R.[1], Agostini V.[1], Garajova I.[1], Biasco G.[1], Ficorella C.[2]

[1]Department of Hematology and Oncological Sciences L. and A. Seragnoli, Policlinico Sant'Orsola Malpighi, University of Bologna, Bologna, Italy; [2]Medical Oncology, S. Salvatore Hospital, University of L'Aquila

Background. Although Folfoxiri as induction chemotherapy demonstrated to be efficient in long term outcome, its therapeutic use was limited by toxicity concerns. We believe that triplets schedules are to be implemented in clinical practice to find a tolerable and effective outcome.

Methods. We collected data from 2 groups; group A received a weekly administration of alternating irinotecan 180 mg/m^2 or oxaliplatin 80 mg/m^2 associated 5FU 900 mg/m^2 in first-line; Group B received FOLFOXIRI (according Masi et al, Ann Oncol, 2004) in second/third-line.

Results. Group A: 36 patients, 22 males (61%), median age 62 yrs (39-74), age >64 14 pts (39%); ECOG 1-2 = 6 pts (17%); haematologic toxicity: G1 = 3 pts (13%), G2 = 15 pts (65%), G3 = 5 pts (22%), G4 = 0 pts. Non-haematologic toxicity: G1 = 4 pts (17%), G2 = 9 pts (39%), G3 = 2 pts (9%), G4 = 1 pt (4%). Group B: 49 patients; 31 males (63.3%), medium age 65 years (47-84), age >64 25 pts (49%), ECOG = 1-2 17 pts (34.7%). Second-line = 18 pts (37%), third-line = 31 pts (63%). Median dose-intensity: 5-FU = 1268 mg/m^2/w, oxaliplatin = 33 mg/m^2/w, irinotecan = 64 mg/m^2/w. Second vs third-line: median OS 10.37 vs 9.33; p = 0.21 and median PFS 8.33 vs 5.17; p = 0.0036. Haematologic toxicity: G1 = 11 pts (22%), G2 = 10 pts (20%), G3 = 11 pts (22%), G4 = 12 pts (24%). Non-haematologic toxicity: G1 = 8 pts (16%), G2 = 18 pts (37%), G3 = 6 pts (12%), G4 = 2pts (4%). A subgroup of patients >65 yrs (25) showed a higher incidence of G3-4 haematologic toxicity (69.6% vs 33.3%; p = 0.033) but not in non-haematologic toxicity or in OS [9.23 (age >64) vs 10.43; p = 0.08] and PFS (6.37 vs 6.27; p = 0.17).

Conclusions. The mCRC triplets schedules, both in front and subsequent lines, showed toxicity pattern comparable with doublet which is known to be effective in these patients; therefore this approach could be increasingly integrated into clinical practice.

E33 NASAL SEPTUM DISORDERS DUE TO BEVACIZUMAB: A CONSECUTIVE SERIES FROM A SINGLE INSTITUTION

D'Amico M.[1], Pagano M.[2], Pasa A.[1], Puntoni M.[1], Gennari A.[1], Zanardi S.[1], Gozza A.[1], Caroti C.[1], Africano R.[2], Defferrari C.[1], De Censi A.[1]

[1]S.C. Oncologia Medica, [2]S.C. Otorinolaringoiatria, E.O. Ospedali Galliera, Genova

Background. Nasal septum is a vulnerable zone which may be damaged by different vascular disorders. The association between nasal septum perforation and bevacizumab has recently been reported. We assessed the frequency and severity of nasal septum alterations during bevacizumab treatment and which factors may contribute to the onset of this adverse effect.

Patients and methods. We conducted an observational study from June 2010 to March 2011 in 29 consecutive patients (28% males, 72% females; median age 56 years; median PS ECOG: 0) suffering from advanced cancers who were treated with bevacizumab plus chemotherapy. The dose was either 5 mg/kg (41.4%), or 7.5 mg/kg (24.1%) or 10 mg/kg (34.5%) q14 (48.3%) or q21 (51.7%). All patients underwent complete ENT examination. The use of cocaine was excluded in all patients.

Results. The median number of cycles at ENT examination was 8; 44.8% of subjects were accustomed to intranasal digital manipulation. Twenty-eight patients developed mucosal lesions (monolateral 17.9%, bilateral 82.1%), associated with dyschromia in 50% or erosion in 35.7%. One patient developed septal perforation. The lesions were multicentric in 11 cases and associated with epistaxis (grade 1-2) in 18; the median diameter of lesions was 10 mm. Nasal cavity/paranasal sinus reactions (grade 1, 2 or 4) were noted in 17 cases. Bevacizumab was not discontinued in any case due to septal disorders. No significant correlation between nasal septum toxicity and tumour response, type of chemotherapy and bevacizumab duration was observed, whereas there was a higher risk of grade ≥2 nasal events with the 7.5 mg/kg dose (OR = 20.9, p = 0.041, adjusted for age and gender).

Conclusions. We found a high incidence of nasal septum lesions in patients receiving bevacizumab plus chemotherapy, irrespective of chemotherapy regimen. Most cases had low grade disorders, but severe toxicity resulting in function alterations may occur. The only significant factor associated with higher risk of this adverse event is a dose of 7.5 mg/kg. Our study is ongoing to further characterize the magnitude of this event.

E34 PROSPECTIVE EVALUATION OF IMPACT OF SKIN TOXICITY ON QUALITY OF LIFE IN ELDERLY PATIENTS WITH METASTATIC COLORECTAL CANCER TREATED WITH CETUXIMAB

Tonda L., Gaspari F., Sirgiovanni M.P., Vana F., Pontiglio E., Vietti Ramus G.

Oncologia Medica, Ospedale San Giovanni Bosco, Torino

In randomized clinical trials elderly patients are underrepresented and data about toxicity and/or quality of life (QoL) are often not age-stratified. Effectiveness and safety of cetuximab treatment in elderly patients (pts) with metastatic colorectal cancer (MCRC) was retrospectively evaluated in a large cohort of

European patients, and in subgroup analysis of prospective randomized studies. There are few data about the impact of this treatment on QoL.

From April 2010 to April 2011 we prospectively evaluated skin-toxicity related QoL in 15 consecutive pts aged >70 yrs treated with cetuximab for MCRC in our outpatient clinic. After one month of cetuximab therapy skin toxicity was recorded using the CTC NCI 3.0 version and QoL was evaluated using the Dermatology Life Quality Index (DLQI) Italian version. Relationship between cumulative skin toxicity scoring and QoL impact was evaluated with linear regression testing and Anova testing.

Mean age was 74.5 yrs ± 4.5. Two were female pts and 13 male. No patients had previous history of skin illness. Rash and desquamation were detected in all pts (9 G1 and 6 G2), xerosis in 13 pts (12 G1 and 1 G2), nail changes in 5 pts (all G1), hitching in 7 pts (all G1). No skin toxicity >G2 was recorded. Global toxicity score was obtained adding single item scores. DLQI global score showed a small effect of skin toxicity on QoL in 9 pts, a moderate effect in 6 pts and a large effect in no patient. The most affected headings were 'symptoms and feelings' and 'daily activities'. Less important was the impact on 'leisure' and 'personal relationships' and 'work and study'. No relationship was found between toxicity scoring and DLQI scoring.

Skin toxicity after one month of cetuximab therapy in this elderly group of pts was similar to that previously reported in no age-selected population. The lack of severe toxicity may be due to the short duration of therapy when data were recorded and also to the use of prophylactic treatment with UV-filters and skin-moisturizers. DLQI is probably less effective for QoL evaluation in elderly people because it emphasizes some life aspects (work and social relationships) less important in this group than in younger people. Despite this, our data seem to confirm not only the good toxicity profile of cetuximab in elderly people but also its tolerable impact on QoL.

E35 BRAIN METASTASES (BM) FROM COLORECTAL CANCER (CRC): A SINGLE INSTITUTION EXPERIENCE

Pietrantonio F.[1], Biondani P.[1], Fantini S.[2], Buzzoni R.[1], Valvo F.[2], Santini M.G.[1], Colonna V.[1], Dotti K.F.[1], Di Bartolomeo M.[1]

[1]Medical Oncology Unit, [2]Radiology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Background. BM from CRC are rare (2-4%) and median survival (MS) is dismal (3 months), mainly due to late diagnosis, extensive systemic disease, treatment refractoriness, cerebellar involvement and poor performance status. Although brain imaging is not routinely performed in metastatic CRC, better patients (pts) survival will likely result in increased BM incidence.

Patients and methods. A retrospective analysis was performed on CRC pts with BM treated at a single Institution, in order to collect data about clinical features and outcome. Radiation Therapy Oncology Group recursive partitioning analysis (RPA) was used to assess prognosis.

Results. From January 2005 to April 2011, 26 consecutive CRC pts with BM were treated at the National Cancer Institute of Milan. All were diagnosed for neurologic symptoms. Median age 60 years (range 41-85), M/F:12/14, 13 (50%) solitary BM, 12 (46%) supratentorial, 7 (27%) cerebellar and 7 (27%) both, mean diameter 27 mm. Twenty (77%) pts had progressive pulmonary disease, 10 (38%) mediastinal involvement, 19 (73%) multiple metastatic sites and only 4 (15%) isolated brain progression. Median time from primary diagnosis and from thoracic metastases to BM was 3 years and 27 months, respectively. Six patients (23%) were treated with surgery and adjuvant/salvage radiation: all had single BM, with younger age and controlled/absent extracranial disease; twenty (77%) pts received radiotherapy alone, either stereotactic, whole brain or both. MS for the overall population was 16.5 weeks; 6-month survival, 34%. MS according to treatment: surgery plus adjuvant/salvage radiotherapy: 12.5 months; radiotherapy alone: 6 weeks. MS according to RPA: class I, 52 weeks; class II, 28 weeks; class III 2 weeks.

Conclusions. Diagnosis of BM from CRC is often late and prognosis is extremely poor. RPA III pts should be treated with supportive care alone, while selected RPA I pts can benefit from multimodality treatments. Brain imaging in plurimetastatic CRC pts should be done starting 2 years after initial diagnosis of lung metastases and in case of progressive thoracic disease.

E36 SPHINGOSINE KINASE 1 (SPHK1) CONTRIBUTES TO RESISTANCE TO EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) INHIBITORS IN COLORECTAL CANCER MODELS

Nappi L.[1], Rosa R.[1], Damiano V.[1], Formisano L.[1], Gelardi T.[1], D'Amato C.[1], Marciano R.[1], De Maio A.P.[1], Ferrara R.[1], Tortora G.[2], Veneziani B.M.[3], De Placido S.[1], Bianco R.[1]

[1]Dipartimento di Endocrinologia ed Oncologia Molecolare e Clinica, Laboratori di Terapia Medica dei Tumori, Università Federico II Napoli; [2]Cattedra di Oncologia Medica, Università di Verona; [3]Dipartimento di Biologia e Patologia Cellulare e Molecolare "L. Califano", Università Federico II di Napoli

Background. Although EGFR targeted agents represent an effective strategy in the treatment of several cancer types, including colorectal cancer (CRC), the clinical use of these agents is significantly limited by intrinsic or acquired resistance. Alterations in the 'sphingolipid rheostat', or the balance between the proapoptotic molecule ceramide and the mitogenic factor sphingosine-1-phosphate (S1P), due to overactivation of sphingosine kinase 1 (SphK1), have been involved in the regulation of resistance to both chemotherapeutics and targeted agents.

Experimental plan. Since some studies have described cross-talks between SphK1 and EGFR-dependent signalling pathways, we investigated the involvement of SphK1 in resistance to EGFR inhibitors in CRC models.

Results. We used CRC cell models with both intrinsic or acquired resistance to the anti-EGFR monoclonal antibody cetuximab. We found that SphK1 is overexpressed in CRC cells resistant to EGFR inhibitors. Consistently with this data, higher doses of N, N-dimethylsphingosine (DMS), a potent competitive inhibitor of SphK1, are needed to achieve complete enzyme saturation and survival inhibition in resistant cells. Moreover, ceramide induces apoptosis less efficiently in resistant than in sensitive cells, consistently with the idea that increased SphK1 levels mediate S1P synthesis by ceramide in resistant cells. The contribution of SphK1 to the resistant phenotype was supported by the demonstration that SphK1 inhibition by DMS or silencing via siRNA in resistant cells restores sensitivity to anti-EGFR drugs, whereas exogenous SphK1 overexpression in wild-type cells confers resistance to these agents. Finally, treatment of resistant CRC cells with fingolimod (FTY720), a S1P receptor inhibitor,

resulted in re-sensitization to cetuximab even in presence of KRAS mutation. We are now investigating the correlation between SphK1 expression in tissue samples derived from CRC patients with KRAS mutations and response to cetuximab.

Conclusions. Our data could contribute to clarify the role of SphK1 in the onset of resistance to EGFR inhibitors and they may suggest SphK1 inhibition as a part of novel targeting strategies potentially effective also in resistant cancer patients.

E37 TOLERABILITY AND QUALITY OF LIFE IN ELDERLY PATIENTS TREATED WITH BEVACIZUMAB FOR METASTATIC COLORECTAL CANCER

Mocerino C., Taddeo M., Gambardella A.

5th Division of Internal Medicine, A.O.U. Policlinico, Second University of Naples, Naples, Italy

Introduction. The use of bevacizumab, anti-VEGF monoclonal antibody, in combination with regimens based on 5FU/LV (or capecitabine) ± irinotecan or oxaliplatin, considerably improved prognosis of patients with metastatic colorectal cancer (mCRC). However, potential adverse events such as hypertension, proteinuria, bleeding, gastrointestinal perforation and thrombosis should be considered especially in elderly patients. Aim of our study was to assess bevacizumab-related adverse events and their influence on quality of life in two groups of patients with mCRC.

Patients and methods. From January 2008 to June 2010 we studied 59 patients with mCRC, receiving first-line chemotherapy plus bevacizumab (5 mg/kg every 2 weeks), divided in two groups, the first of 28 patients aged ≤70 years (range 35-70; mean 58.4 years) and the second of 31 patients >70 years (range 71-79; mean 72.7 years). Patients with impaired renal function and/or proteinuria ≥0.5 g/day were excluded. Adverse events were defined according to the National Cancer Institute Common Terminology Criteria (NCI-CTCAE v3.0.) Quality of life was assessed with FACT-C, EORTC-C30 and CR38 questionnaires. Patients were evaluated at baseline, at each cycle of therapy, three and six months after the end of chemotherapy.

Results. Any grade hypertension occurred in 7 (25%) patients ≤70 years and in 9 (29%) older patients. Grade 3 hypertension, requiring the initiation or a change of antihypertensive therapy, was observed in 3 (10.7%) patients ≤70 years and in 4 (12.9%) patients >70 years. Proteinuria occurred in 8 (28.6%) patients ≤70 years and in 9 (29%) older patients. Grade 4 hypertension (hypertensive crisis) and/or grade 4 proteinuria (nephrotic syndrome) was not seen. The FACT-C and EORTC questionnaires showed that bevacizumab-related side effects had no impact on quality of life.

Conclusion. In our study combination therapy with bevacizumab was well tolerated with a generally manageable safety profile in all patients. Bevacizumab-related adverse events such as hypertension and proteinuria, while noting more prevalent in patients aged >70 years, had no significant effects on quality of life.

E38 SAFETY OF BEVACIZUMAB PLUS CHEMOTHERAPY IN METASTATIC CANCER PATIENTS: AN EXPERIENCE IN UNSELECTED POPULATION

Tagliabue P., Aglione S., Beretta E., Facendola G., Ferrario A., Mastore M., Nova P., Panzarino C., Pozzi P., Toffolatti L., Verga M., Fagnani D.

Oncology Department, A.O. di Desio e Vimercate (MB)

Background. Bevacizumab, a humanized monoclonal antibody inhibiting VEGF tumour angiogenetic activity, was approved, in combination with chemotherapy, for treating many types of advanced cancer. Because of the important role of VEGF in vascular function and physiological angiogenesis its inhibition by bevacizumab has been noted to cause serious adverse events, including bleeding, thromboembolic events, bowel perforation and neutropenia.

The aim of this observational retrospective study was to evaluate the safety and the toxicity profile of bevacizumab in addition to several chemotherapeutic regimens in advanced cancer.

Materials and methods. From January 2006 to April 2011, 89 patients with metastatic cancer (84 colorectal, 3 renal, 1 breast, 1 lung) were treated with bevacizumab, in addition to different chemotherapeutic regimens (74 patients CPT11+5FUic, 6 FOLFOX4, 4 degramont, 1 paclitaxel, 1 carboplatin-paclitaxel, 3 interferon) in Medical Oncology Department of Azienda Ospedaliera di Desio e Vimercate. Eighty-five (96%) patients received bevacizumab as first-line chemotherapy and 4 (4%) as second-line. The G3-G4 toxicities were recorded according to WHO classification system. Results are based on descriptive analysis of the first toxicity event.

Results. Overall G3 and G4 toxicities were reported in 24 patients (27%). Adverse events leading to treatment discontinuation were recorded in 7 patients (7.8%). One death occurred, due to a thromboembolic event (1.1% fatal event).

Type of ADR	No. G3-G4 ADR (%)	Treatment discontinuation (%)
Hypertension	13 (14.60%)	1 (1.1%)
Bleeding	3 (3.40%)	1 (1.1%)
Thromboembolic events	2 (2.20%)	3 (3.4%)
Other events	GI disorders 3 (3.4%) Myelotoxicities 2 (2.2%) Cardiac disorders 1 (1.1%)	2 (2.2%)

Conclusions. According to our experience, bevacizumab plus chemotherapy seems to be a well tolerated treatment in clinical practice, and its safety profile in addition to chemotherapy appears consistent with those reported by other experiences. Hypertension, the most common adverse event, was well manageable and leaded to treatment discontinuation only in one case. Data suggest particular attention to thromboembolic events, being the most frequent cause of treatment discontinuation.

E39 VALUE OF VIDEOLAPAROSCOPY FOR SELECTION OF PATIENTS WITH PERITONEAL CARCINOMATOSIS FROM COLORECTAL CARCINOMA BEFORE CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY

Sassaroli C.[1], Cassata A.[1], Ruffolo F.[1], Bianco F.[1], Scala D.[1], Ottaiano A.[1], Nasti G.[1], Romano C.[1], Tafuto S.[1], Busto G.[2], Tortoriello A.[3], De Franciscis S.[1], Romano G.[1], Iaffaioli R.V.[1]

[1]Department of Abdominal Oncology, National Cancer Institute, Fondazione "G. Pascale", Naples, Italy; [2]Department of Oncology and Hematology, Hospital "Umberto I", Nocera Inferiore, Italy; [3]Department of Medical Oncology, "D. Cotugno" Hospital, Naples, Italy

Introduction. Cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) is a treatment option for peritoneal surface malignancy (PC) from colorectal cancer (CRC). The imaging techniques (TC, RM and PET) are often inadequate to find small lesions of peritoneal surface. TC, RM and PET are useful to exclude metastatic distant disease. A recent consensus statement describes videolaparoscopy (VLS) as a staging step prior to cytoreductive surgery. The extent of peritoneal deposits was quantified and recorded using the Peritoneal Cancer Index (PCI) described by Jacquet and Sugarbaker. PCI obtained at VLS may prospectively help in patient selection avoiding useless surgical procedures.

Methods. Records of eleven patients, with diagnosis of CRC and increase of CEA and/or CA 125, with imaging indicating a PCI ≤20, who underwent laparoscopy for staging from May 2010 until February 2011 were reviewed. Standard VLS technique was performed with: ascites fluid collection for cytopathology, evaluation of PCI index data for all abdominal quadrants; specimen collection for definitive hystopathology. Assessment of PCI was performed in patients who underwent cytoreductive surgery and HIPEC and compared with laparoscopic PCI obtained before major surgery.

Results. All patients had successful visualization of carcinosis. PCI index was estimated ≥20 in 4 pts and ≤20 in 7. Of these seven patients two were found to have metastatic abdominal retroperitoneal adenopathy at laparotomy and were both considered unresectable. Five patients with PCI ≤20 underwent CRS and HIPEC. In all patients, CRS was complete (completeness of cytoreduction, CCR-0/1).

Conclusions. The VLS should be considered a fundamental procedure for correct staging of PCI before peritonectomy and HIPEC. In our experience VLS avoided six major laparotomic procedures in patients who were downstaged at traditional imaging. The extent of lymphatic involvement remains difficult to assess at laparoscopy and should be confirmed at laparotomy.

E40 METASTATIC COLORECTAL CANCER (MCRC) PATIENTS (PTS) TREATED WITH A BI-WEEKLY ADMINISTRATION OF CAPECITABINE + OXALIPLATIN (XELOX-2) + BEVACIZUMAB: COULD VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) FREE LEVELS BE A PREDICTIVE FACTOR?

Silvestris N.[1], Azzariti A.[2], Porcelli L.[2], Quatrale A.E.[2], Paradiso A.[2], Colucci G.[1]

[1]Medical and Experimental Oncology Unit, [2]Clinical and Experimental Oncology Laboratory, IRCCS National Cancer Institute, Bari, Italy

Background. Serum VEGF has been proposed as a surrogate biomarker for bevacizumab activity even if literature data are conflicting. Our study deepened the hypothesis that VEGF levels in immunodepleted plasma of mCRC pts could be a possible pharmacodynamic marker for this drug.

Methods. We evaluated previously untreated mCRC pts receiving 4 cycles of XELOX-2 regimen (Fedele et al., ASCO 2009) in combination with bevacizumab (5 mg/kg on day 1 q2w). The determination of VEGF levels, total and free (meaning after immunodepletion of plasma samples) were measured at baseline and the days before the 2nd and the 5th cycle.

Results. Four patients treated as above described and 3 pts treated with adjuvant FOLFOX-4 regimen (control arm) were considered. We observed that free VEGF levels significantly decreased from baseline to day 14 and 74 of bevacizumab treatment of about 40% and more than 50% in all patients with partial response. In 3 patients with stable disease, the baseline level of VEGF free was lower with a decrease of 51% at 14 and 74 days. Conversely, the determination of total VEGF showed a slight reduction of its level (max 20%) after 14 and 74 days and an increase of about 30% in two samples (after 74 days) (Table 1). Analysis in pts receiving FOLFOX-4 regimen showed no significant variation among samples.

Conclusions. These preliminary results can suggest that the measure of baseline circulating free VEGF levels may be useful as a predictive biomarker for bevacizumab-based treatment, with more efficacy when it is higher. The evaluations of other 3 pts will be ready within one month.

Table 1

	VEGF levels (pg/mL) Baseline		VEGF levels (pg/mL) Before the 2nd cycle		VEGF levels (pg/mL) Before the 5th cycle		Response to treatment
	free	total	free	total	free	total	
Pt 1	188.5	230	117.5	171.25	92.5	207.5	PR
Pt 2	128.75	152.5	77.5	150	77.5	206.25	SD
Pt 3	182.5	255	98.75	223.75	58.75	197.5	PR
Pt 4	185.5	240	101.5	212.75	83.5	213.5	PR
Control 1	140	200	126.25	205			
Control 2	226.25	227.5	212.5	206.25			
Control 3	230.75	235	225.5	228.5			

PR: partial response; SD: stable disease.

E41 THE SAFETY AND TOLERABILITY OF CAPECITABINE IN ELDERLY CANCER PATIENTS: A RETROSPECTIVE ANALYSIS

Luciani A., Dottorini L., Di Maria G., Bertuzzi C., Crepaldi F., Broggio F., Caldiera S., Ferrari D., Foa P.

Background. Capecitabine (Xeloda) is a fluoropirimidine analog approved for the treatment of breast and gastrointestinal tumours. Capecitabine is an oral drug and data from phase II and III trials showed a good toxicity profile in selected populations. As there is a paucity of elderly-dedicated clinical trials in literature, we performed a retrospective study in older population to analyze the tolerability and feasibility of capecitabine monochemotherapy.

Patients and methods. Clinical charts of elderly patients referred to our department since 2004 were reviewed. Inclusion criteria for the analysis were: age 70 years or more, diagnosis of breast or colorectal cancer, treatment with capecitabine as monotherapy. For all patients, age and stage disease at the beginning of treatment, number of comorbidities, polypharmacy, CIRS-G (Cumulative Illness Rating Scale for Geriatrics) score and index, ADL (Activities of daily living) and IADL (Instrumental Activities of Daily living) and response to treatment were available. Descriptive statistics was calculated. Two logistic re-

gression analyses exploring the variables influencing dose reduction and those influencing the risk of death were performed.

Results. Thirty-eight patients (pts), 18 females and 20 males (47 and 53%) were considered. Mean age was 78 years (range 71-88, SD 4.6). 84% (32/38) of diagnosis were colorectal cancer and 16% (6/38) breast cancer; 60% (23/38) of pts had stage IV disease. Patients were not pretreated. Mean number of cycles was 4.6 (range 1-12), 26% (10/38) of pts had dose reduction and 24% (9/38) interrupted prematurely the treatment. 31% (12/38) of pts had a partial response or disease stabilization. Overall, schedule modifications occurred in 50% of patients (19/38). The main causes were toxicity (18%, 7/38) and patients' refusal (8%, 3/38). No toxic deaths or febrile neutropenia events occurred. The main toxicities were as follows: fatigue 16%, diarrhoea 10%, mucositis 8%, nausea 8% and hand/foot syndrome 5%. In the logistic regression analysis polypharmacy ($p = 0.02$, OR 1.8, 95% CI 1.08-3.08) and IADL ($p = 0.01$, OR 3.1, 95% CI 1.4-7) were significantly associated with schedule modification. Age was the only factor influencing the risk of death ($p = 0.012$; OR 1.26, 95% CI 1.05-1.52).

Conclusions. In our experience half of patients treated with capecitabine required schedule modifications mainly for toxicity. Geriatric impairments as well as polypharmacy should be taken into account carefully before treating these patients. These parameters should be further evaluated in the context of a prospective clinical trial.

E42 BRACHIAL ARTERY (ba) FLOW-MEDIATED DILATION (FMD) TEST MAY DETECT ENDOTHELIAL DYSFUNCTION IN PATIENTS TREATED WITH STANDARD FLUOROURACIL/IRINOTECAN/BEVACIZUMAB (FOLFIRI-B) CHEMOTHERAPY

Formica V.[1,2], Rodia G.[3], Grenga I.[1], Martano L.[1], Lauro R.[3], Roselli M.[1,2], Tesauro M.[3]

[1]Medical Oncology Unit, Tor Vergata Clinical Center, University of Rome; [2]IRCCS San Raffaele Pisana, Rome; [3]Internal Medicine Department, Tor Vergata Clinical Center, University of Rome

Background. Chemotherapy regimens, especially the bevacizumab-containing ones, may determine relevant cardiovascular toxicity and arterial thromboembolic events (ATEs) are observed in up to 10% of patients treated with FOLFIRI-B. ba-FMD is calculated by high-resolution ultrasound as the percentage dilation of brachial artery diameter from baseline following 10 min of forearm cuff occlusion (post-ischemia response) and is widely used to assess health of the vascular system. It reflects endothelial function and when impaired it is associated with an increased risk of ATEs. We investigated whether FOLFIRI-B was associated with altered ba-FMD in metastatic colorectal cancer (mCRC) patients.

Methods. A cross-sectional study including mCRC patients on standard first-line biweekly FOLFIRI-B was started to assess endothelial function in this setting of patients by means of standard ba-FMD analysis.

Results. Ten patients have so far been included (study commencement: April 2011), 7 males and 3 females, median age 67 (range 57-81). Number of treatment cycles administered was significantly associated with ba-FMD with significant dilation impairment (i.e. FMD <5%) for all patients who received more than 10 cycles of therapy (7 patients, mean baseline artery diameter 38 mm, mean FMD 0.86%, range 0-3.3%, mean number of FOLFIRI-B cycles 19, range 10-33) as compared with patients receiving 9 cycles or less who all demonstrated an FMD >5% (3 patients, mean baseline artery diameter 40 mm, mean FMD 8.03%, range 5.70-11.1%, mean number of cycles 6, range 3-9), Fisher's exact test p value 0.008, odds ratio 105.0, 95% CI 1.7-6465.1. No ATEs have so far been recorded, no significant associations with treatment efficacy outcomes have been demonstrated, though median follow-up is still limited (9.2 months).

Conclusions. Although larger sample size and longer follow-up are required to draw definitive conclusion on the association between impaired ba-FMD and ATEs risk, our preliminary results show for the first time that duration of FOLFIRI-B treatment is associated with impaired endothelial function as measured by standard non-invasive ba-FMD.

E43 CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY WITH OXALIPLATIN FOR THE TREATMENT OF ISOLATED PERITONEAL CARCINOMATOSIS FROM COLORECTAL CARCINOMA

Cassata A.[1], Sassaroli C.[1], Delrio P.[1], Ottaiano A.[1], Romano C.[1], Nasti G.[1], Tafuto S.[1], Maiolino P.[2], Cremona F.[1], Pace U.[1], Busto G.[3], Iaffaioli R.V.[1], Romano G.[1]

[1]Department of Colorectal Oncology, National Cancer Institute, Fondazione "G. Pascale", Naples, Italy; [2]Hospital Pharmacy, National Cancer Institute, Fondazione "G. Pascale", Naples, Italy; [3]Department of Oncology and Hematology, Hospital "Umberto I", Nocera Inferiore, Italy

Background. Peritoneal tumour dissemination from colorectal cancer (CRC) is a sign of advanced tumour stage or disease recurrence and mostly associated with poor prognosis. In the last twenty years, surgery and chemotherapy have been combined to help to increase the survival rate decreasing the spread of peritoneal disease. Our objective was to determine if cytoreductive surgery (CRS) followed by hyperthermic intraperitoneal chemotherapy with oxaliplatin (HIPEC) is a feasible therapeutic option for treatment of peritoneal carcinomatosis (PC) from CRC.

Methods and results. Between May 2010 and September 2010, five patients with PC confined to the peritoneal cavity underwent CRS with HIPEC. HIPEC was administered (using the closed abdomen technique) intraperitoneally with oxaliplatin 460 mg/m^2 at a average temperature of 42.5 °C over 30 minutes. Before the beginning of HIPEC, and during CRS, all patients had received intravenous fluorouracil 400 mg/m^2 and leucovorin 20 mg/m^2. All patients underwent laparoscopy for determining the PCI (peritoneal cancer index) before CRC and HIPEC (median value of PCI was 13). Histopathological mucinous type was found in three patients. In all patients, CRS was complete (completeness of cytoreduction, CCR-0/1). Three patients are alive with good performance status (two are disease-free and one with hepatic recurrence), two patients died (one for disease progression). Regarding the major complications of the procedure (grades 3 and 4 according to the National Cancer Institute Common Toxicity Criteria) they occurred in 2 patients (prolonged hepatic impairment and fever resistant), and no patients underwent reoperation. The median duration of hospitalization was 19 days (range 14-28 days).

Conclusion. CRS and HIPEC is a combined treatment strategy for only selected patients with PC that can improve overall

survival. The PCI and the CCR score are the leading predictors of postoperative patient outcome. In conclusion, highly selected patients with CRC confined to the peritoneal cavity may benefit from improved survival after CRS with HIPEC.

E44 HEMANGIOBLASTOMA OF THE GASTROINTESTINAL TRACT

Casadei Gardini A.[1], Pieri F.[3], Fusaroli P.[2], Passardi A.[1], Monti M.[1], Rosetti P.[1], Calpona S.[1], Valgiusti M.[1], Ragazzini A.[1], Ricci M.[1], Frassineti G.L.[1]

[1]Istituto Scientifico Romagnolo per lo Studio e Cura dei Tumori, Meldola (FC), Italy; [2]Department of Clinical Medicine, GI Unit, University of Bologna/ Hospital of Imola, Italy; [3]Pathology Unit, Morgagni-Pierantoni Hospital, Forlì, Italy

We present the first documented case of hemangioblastoma located in the left gastrointestinal tract in a 75-year-old woman. In May 2009, the patient, whilst undergoing adjuvant chemotherapy for breast cancer (pT2, pN2a M0), reported rectal bleeding, which caused significant anemia (Hb = 7.8 g/dL). Colonoscopy was performed, revealing a roundish mass covered with normal mucosa at the level of the sigmoid colon; the remaining colon was normal. Endoscopic biopsies of the mass were unrevealing. Endoscopic ultrasound (EUS) was performed using a 12 Mhz miniprobe, showing a isoechoic lesion originating from the 3rd layer of the wall (submucosa) while the underlying layers were normal. The lesion was 14 x 11 mm in size and its echotexture was homogeneous. As the EUS aspect was not strongly suggestive either of cancer or malignant stromal tumour, follow-up was advised. At 6-month follow-up, both endoscopic and EUS pictures were unchanged. Subsequently, due to repeated lower gastrointestinal bleeding episodes, the patient underwent left hemicolectomy in October 2010.

Grossly a sharply circumscribed submucosal yellowish nodule of 13 mm was observed which was not attached to any peripheral nerve.

Histologically, the lesion was composed of large, atypical cells traversed by a network of blood vessels. Numerous cells had highly pleomorphic nuclei and a finely vacuolated cytoplasm. Immunohistochemically, the cells showed strong positivity for inhibin and NSE and weak positivity for S-100. A diagnosis of hemangioblastoma of the gastrointestinal tract was made. Given the rarity of this tumour and the patient's history of breast cancer, genetic studies will be carried out to identify possible gene mutations. The diagnosis is based on the presence of typical morphology and immunophenotype. The recognition of hemangioblastoma depends in large part upon awareness of the lesion but it is so rare in extraneural sites that it is highly probable that this neoplasm may not even be included as a differential diagnosis.

Probably this diagnosis must be take in consideration submucosal bleeding lesions.

E45 UNUSUAL CLINICAL COURSE OF COLORECTAL CANCER

Miele E.[1], Spinelli G.P.[2,3], Lo Russo G.[2,3], Codacci Pisanelli G.[2,3], Vari S.[2], Papa A.[2], Zoratto F.[2], Stati V.[2,3], Ferrari A.[2], Zaccarelli E.[2], Tomao S.[2,3]

[1]Department of Experimental Medicine, Sapienza University of Rome; [2]Department of Medical-Surgical Science and Biothecnology, Oncology Unit, S. Maria Goretti Hospital, Latina - Sapienza University of Rome; [3]Distretto ASL, Aprilia - Oncology Unit, Sapienza University of Rome

Introduction. Dukes A stages of colorectal cancer are rarely reported to metastasize. Subcutaneous metastases from colorectal carcinoma are rare events and usually indicate widespread disease. Here we present a patient's case with a Dukes A colorectal cancer at diagnosis and relapsing three years later with a single subcutaneous lesion.

Case report. In August 2007 a 72-year-old woman underwent a right hemicolectomy for a Dukes A colon cancer (staging pT2, pN0 [0/27nodes], G2). Computed tomography (CT) of abdomen-pelvis and chest did not show distant metastases, so she was no further treated. The patient remained asymptomatic up to May 2010 and follow-up findings did not suggest recurrence. In June 2010 she acutely presented a painless swelling affecting the left paravertebral dorsal region skin. Tumour serum markers were not increased and a colonoscopy did not show local disease relapse. A chest X-ray excluded pulmonary metastasis and abdominal ultrasound did not detect either liver metastases or peritoneal dissemination. Thus ultrasound scan to the dorsal mass was performed and a suspect heterogenous solid vascularized lesion was described. Thus patient underwent a radical en-bloc resection of the dorsal swelling. Histological analysis of the excised specimen showed metastatic poorly differentiated adenocarcinoma, originated from large bowel, infiltrating the skin and subcutaneous tissue. A total body CT (TB-CT) confirmed no evidence of visceral metastases. At present, the patient is treated with FOLFIRI schedule and she remains asymptomatic.

Conclusion. This case history describes a rare pattern of colon cancer metastasis. In a biological perspective this case outlines the poly-phenotypic nature of cancer: the course of disease that we report here is clearly determined by a peculiar cancer cell population with specific biology and homing. Progresses in molecular biology are strongly warranted to distinguish patients with peculiar clinical course and prognosis. The unusual and aggressive history of this disease stresses the importance of intensive follow-up also in patients with good prognostic factors.

E46 PRELIMINARY DATA ON THE PROPHYLACTIC USE OF THE CREAM CONTAINIG UREA AND VITAMIN K1 (VIGORSKINK1®) TO PREVENT SKIN TOXICITY BY CETUXIMAB

Calista F.[1], Silvestri A.[2], Assalone P.[1], Tomei F.[1], Traficante D.[1], Antuzzi G.[2], Carrozza F.[2], Giglio G.[2], Musacchio M.[2], Di Lullo L.[1,2]

[1]ASReM, U.O.C. Oncologia, Ospedale Veneziale, Isernia; [2]ASReM, U.O.C. Oncologia, Ospedale Cardarelli, Campobasso

Background. Skin toxicity, including acne like rush, xerosis, hair growth disorders, pruritus, desquamation and nail changes, is the major side effect associated with cetuximab treatment. Skin toxicity can severely impact patients physical, psychological and social wellbeing and can lead to discontinuation of treatment or dose reduction. Therefore the effective management of skin toxicities is essential to maximize treatment efficacy and maintain quality of life. Preclinical studies have shown that vitamin K reactivates EGFR mediated signal transduction after the inhibition via EGFR receptor antagonists. To date, no data have been published on the use of prophylactic vitamin K based cream to prevent skin toxicity by cetuximab. The aim of our study, we present preliminary data, is to demonstrate the effectiveness of vitamin K1 in preventing or reducing skin toxicity when used in prophylaxis during cetuximab therapy.

Methods. Between December 2010 and May 2011, 10 patients were treated with the cream containing urea and 0.1% vitamin K1 (VigorskinK1®). Eight patients with metastatic colorectal cancer and two patients with squamous cell carcinoma of the head and neck. Six patients were treated in prophylaxis and four at the onset of skin toxicity (NCI CTCAE version 3).

Results. Forty-five cycles of therapy were administered to patients treated prophylactically. None of the patients had to discontinue treatment. Two patients have completed therapy regularly. No toxicity of grade 3 or 4 was recorded with a patient who developed a G2 toxicity (skin rash) resolved in 4 days. Other toxicities recorded, all G1, include xerosis (2 patients) and paronychia (1 patient). Of the remaining four patients, treated with the onset of toxicity, no one has interrupted treatment; the toxicity recorded (rash, xerosis and paronychia) after the introduction of topical VigorskinK1® was G1.

Conclusion. These preliminary data on the use of preventive cream VigorskinK1 confirm the effectiveness of prophylactic therapy in the treatment of rash induced by treatment with cetuximab. Final data will be presented to the Congress.

E47 CASE REPORT: OVER 20 MONTHS RESPONSE IN A PATIENT TREATED WITH PANITUMUMAB FOR COLORECTAL CANCER

Sponziello F., Nacci A., Calvani N., Mazzoni E., Rizzo P., Orlando L., Schiavone P., Fedele P., Chetrì C., D'Amico M., Marino A., Cinefra M., Cinieri S.

Medical Oncology Division and Breast Unit, Sen. Antonio Perrino Hospital, Brindisi, Italy

In June 2004 a 70-year-old male underwent anterior rectal resection for G1 pT3 pN1(3/6) M0 colorectal adenocarcinoma and then received adjuvant chemotherapy with the De Gramont regimen. In January 2007 he restarted chemotherapy with first-line FOLFOX 4 (only 4 cycles), second-line FOLFIRI (34 cycles) and third-line irinotecan plus cetuximab (since EGFR+ and K-Ras wild type) consecutive regimens due to the onset and progression of liver metastases only. The irinotecan plus cetuximab regimen was characterized by G3 gastrointestinal toxicity after just the first cycle. Irinotecan was suspended and the patient continued treatment with only cetuximab. However, the latter was associated to an important adverse reaction with fever and respiratory symptoms during both the second and third infusion. Thus, we decided to suspend also the cetuximab and start a fourth-line treatment with panitumumab 6 mg/kg iv q2w, which is still ongoing after 42 cycles with a partial response maintained for over 20 months as assessed by CT scans repeated every 3 months. At present the only significant toxicity reported is a manageable G2 skin rash. The patient will continue the treatment with panitumumab until disease progression or unacceptable toxicity.

Session F • Supportive and palliative care

F1* HUMANIZATION OF CANCER CARE (HUCARE): FINAL RESULTS OF A NATIONAL PROJECT AIMED AT THE IMPLEMENTATION OF EVIDENCE-BASED RECOMMENDATIONS IN THE PSYCHOSOCIAL CARE OF ADULT CANCER PATIENTS

Passalacqua R.*, Caminiti C.°, Annunziata M.A.^, Borreani C.^^, Diodati F.°, Fagnani D.°°, Filiberti S.*, Ollari M.G.°, Saleri J.*, Donati G.*, Zerla P.°°, Maddalena R.**, Isa L.**

Istituti Ospitalieri, Cremona; °University Hospital, Parma; ^CRO Aviano; ^^NCI Milan; Oncology Division of °°Vimercate,Gorgonzola, Milan, Italy*

Background. HUCARE is a research project funded by the Ministry of Health and the Lombardia Region. The aim is the implementation, in the oncology centers, of evidence-based medicine (EBM) interventions, aimed at reducing patient psychological distress and improving satisfaction and compliance.

Methods. This is a three-step implementation study: a) context analysis of each participating center aimed at highlighting the difficulties in the implementation; b) introduction of the EBM interventions; c) measuring of compliance. Context analysis has been performed by trained personnel in each center in order to highlight problems and difficulties to the implementation. Interventions were targeted toward three areas: 1. *Communication skills*. It includes specific training courses on communication for doctors and nurses, as well as a question prompt list (QPL) provided to patients during their first visit with the oncologist. 2. *Patient information and education*. Creation of the Point of Information and Support (PIS) inside the center with a shared informative path. Identification of a nurse of reference (NR) for the patient, responsible for providing information and education to each new cancer patient. *3. Psycho-social support*. Measurement of anxiety, depression and social needs of all new patients, who were referred to psychologists or social workers if indicated.

Results. The project began in 33 centers in Italy. Four centers declined to participate after initial adhesion to the project. So far 160 oncologists and 401 oncology nurses have attended the communication courses (17 courses for nurses and 10 for oncologists), representing over 75% of the nursing and medical staff of each center. The 3-day courses were residential and were structured as previously described by Fallowfield L et al. (Lancet, 2002) and defined under the supervision of prof. Fallowfield. Training led to significant improvement of staff skills (evaluated with a pre- post- course test). A QPL developed in Australia was translated and subjected to cross-cultural adaptation, yielding the first validated Italian QPL (Caminiti et al.: BMC Health Serv Res, 2010). 28/29 (96%) oncology centers have created the PIS and 27/29 (93%) have defined an operational manual which specifies the psychosocial care pathway for all new patients treated with chemotherapy. In mid April the final phase of the study began, where the number of patients who actually received the EBM interventions is assessed by examining a sample of clinical charts, during blinded visits in each participating center.

To favour the adoption of these interventions by other oncology centers, a document is being compiled containing practical scientific recommendations for the psychosocial care of cancer patients, promoted by AIOM.

Conclusions. HUCARE is the first study conducted in Italy which introduced into routine clinical practice interventions which were demonstrated by randomized clinical trials to reduce distress of all patients and their families, as they cope with cancer. Strong commitment on the part of oncologists and a support strategy for implementation are required. Final results will be presented at the meeting.

F2* LONG-TERM PROTECTIVE EFFECTS OF THE ANGIOTENSIN RECEPTOR BLOCKER TELMISARTAN ON EPIRUBICIN-INDUCED INFLAMMATION, OXIDATIVE STRESS AND MYOCARDIAL DYSFUNCTION

Mantovani G.[1], Madeddu C.[1], Piras A.[2], Dessì M.[1], Cadeddu C.[2], Deidda M.[2], Massa E.[1], Antoni G.[1], Mercuro G.[2]

[1]Department of Medical Oncology, [2]Department of Cardiovascular and Neurological Sciences, University of Cagliari, Italy

Introduction. Chronic inflammation, oxidative stress and renin-angiotensin system (RAS) play a significant role in chemotherapy-induced cardiotoxicity (CTX): telmisartan (Tel), an antagonist of angiotensin II type-1 receptor, was shown to be able to reduce anthracycline (ANT)-induced CTX.

Patients and methods. We carried out a phase II placebo-controlled randomized trial, to assess the possible role of Tel in the prevention of the cardiac sub-clinical damage induced by epirubicin (EPI). Forty-nine patients (mean age ± SD, 53.0 ± 8 years), cardiovascular disease-free with cancer at different sites and eligible for EPI-based treatment, were randomized to one of two arms: Tel n = 25; placebo (PLA) n = 24. A conventional echocardiography equipped with Tissue Doppler Imaging, Strain and Strain Rate (SR) was performed as well as serum levels of proinflammatory cytokines IL-6 and TNF-α and oxidative stress parameters reactive oxygen species (ROS) and glutathione peroxidase (GPx). All assessments were carried out at baseline, every 100 mg/m^2 of EPI dose and 12-month follow-up (FU).

Results. A significant reduction of the SR peak both in the TEL and PLA arm was observed at t_2 (cumulative dose of 200 mg/m^2 of EPI) in comparison with t_0. Conversely, at t_3 (300 mg/m^2 EPI), t_4 (400 mg/m^2 EPI) and 12-month FU, the SR increased reaching the normal range only in the Tel arm, whilst in the PLA arm the SR remained significantly lower as compared to t_0 (baseline). The differences between SR changes in the PLA and Tel arm were significant from 300 mg/m^2 EPI (t_3) up to 12-month FU. Serum levels of IL-6 increased significantly in the PLA arm at 200 mg/m^2 EPI (t_2) in comparison with baseline but remained unchanged in the Tel arm. The same trend was shown by ROS levels which significantly increased at t_2 versus baseline in the PLA arm, whilst remained unchanged in the Tel arm. The mean change of ROS and IL-6 at t_2 was significantly different between the 2 arms. In the present study, we confirm at 3-month FU the trend toward a decrease of ROS and IL-6 from t_2 in the PLA arm.

Conclusions. Our results suggest that Tel is able to reverse the acute (early) EPI-induced myocardial dysfunction and to maintain later a normal systolic function up to 12-month FU. These effects are likely to be due to different mechanisms: RAS blockade and prevention of chronic inflammation/oxidative stress.

This study was funded by AIRC (Associazione Italiana Ricerca per il Cancro)-project number 8679.

F3* HOME ARTIFICIAL NUTRITION (HAN) IN ADVANCED CANCER PATIENTS: A TWENTY-YEAR ACTIVITY AT ANT FOUNDATION IN BOLOGNA

Ruggeri E., Fettucciari L., Giannantonio M., Agostini F., Pannuti F.

ANT Foundation, Bologna

Background. Malnutrition is over 50% in advanced cancer patients and is related to a decreased survival. The cachexia is the first reason for death in 4-23% of cases, with calculated life expectancy of about 35-40 days.

Aim. To estimate the appropriateness of the criteria to select patients for HAN and the effectiveness of HAN to avoid death from cachexia in patients with advanced cancer assisted at home by ANT Foundation.

Materials and methods. Criteria of patients' selection: inadequate caloric intake ± malnutrition; life expectancy ≥6 weeks; suitable psycho-physical conditions; informed consent. Parameters: sex, age, tumour site, food intake (inadequate: <50% BEE), nutritional status (malnutrition: BMI <18.5), Karnofsky Index (KI), indication for HAN, type of HAN (enteral: HEN, parenteral: HPN), survival after starting HAN. Statistics: m ± sd, Pearson correlation coefficient.

Results. ANT assisted 25,901 patients in Bologna and its province from July 1990 to June 2010. HAN had been submitted to 542 patients (2.1%), 329 M, 213 F (age: 65.5 ± 12.5 yrs), HEN 270/542 (50%), HPN 272/542 (50%). Access route for HEN was: 40% naso-gastric tube, 25% PEG, 33% digiunostomy, 2% gastrostomy; for HPN: 70% non-tunnelled percutaneous catheters, 7% picc, 9% tunnelled, 14% totally implanted ports. Tumour site was: 23% head-neck, 58% gastrointestinal (GI), 5% lung, 8% genitourinary, 6% others. Indication for HAN was: 3% anorexia, 38% dysphagia, 31% upper GI obstruction, 28% lower GI obstruction. All patients died by June 2010. Duration of HAN (weeks) was: HEN, 20.3 ± 24.3; HPN, 15.1 ± 17.1. Survival was ≥6 weeks in 426/542 (79%). Survival was related to KI ($r = 0.291$, $p < 0.0001$).

Conclusions. The low incidence of HAN over all the patients assisted by ANT and the achievement to avoid death from cachexia in 79% of cases prove the efficacy of the criteria of patients' selection in order to prevent excessive and indiscriminate use of HAN. Performance status can be considered a reliable prognostic index and a benefit for the decisional trial in starting HAN.

F4* UNMET NEEDS IN CANCER CONTROL IN DEVELOPING COUNTRIES: REPORT ON THE FIRST YEAR OF ACTIVITIES OF VOLUNTEERS ITALIAN ONCOLOGISTS AT ONCOLOGY DEPARTMENT (OD) OF BUGANDO MEDICAL CENTER (BMC), MWANZA, TANZANIA

Franciosi V., Serra P., Kopf B., Carpi A., La Torre C., Di Lascio S., Iaculli A., Orlandi A., Moscetti L., Nicodemo M., Laudadio L., Di Lullo L., Pfanner E., Puglisi F., Crinò L., Collovà E., Amadori D. on behalf of Associazione Vittorio Tison, Forlì

Background. Cancer outcomes represent an emergency in Tanzania, a low-income country with 42.5 million people, where incidence is 84/100,000 in males and 91/100,000 in females. Nation-wide, there aren't surgeons dedicated to oncology, 7 pathologists, 4 radiation oncologists and only 1 medical oncologist. BMC, Mwanza, has a catchment area of fourteen million people.

Methods. In 2008, a partnership was signed between BMC, Association Vittorio Tison, Istituto Tumori della Romagna (IRST) and Istituto Oncologico Romagnolo (IOR) to realize an OD at BMC (18 beds). According to the project one Tanzanian doctor and three nurses of the staff were trained in oncology at IRST and Italian oncologists, from several Cancer Centers, provided their assistance at OD-BMC, by rotating on a monthly basis.

Results. From February 2010 to April 2011, 14 volunteers oncologists and one data manager, supported the assistance at OD-BMC. The median residence time was 23 days (range 20-30 days). The most frequent tumours in adult females were cervical and breast cancer and lymphomas; in adult males were liver, oesophageal and prostate cancer; in children were Burkitt's lymphoma, retinoblastoma and acute leukemias. Mainly, the oncologists supported the diagnostic and therapeutic decisions, the ward organisation, the doctors and students teaching and the tumour registry implementation. The concerns were: inadequate diagnostic tools (only X-ray and ultra-sound available; frequent clinical and radiological diagnoses, but not pathological); costs and availability of drugs (only cyclofosfamide, methotrexate, 5-fluorouracil and vincristine available and cheap); incorrect oncological pathways (radiotherapy was not available; lack of interdisciplinary discussions; undefined therapeutic purposes; inadequate staging, treatments, response evaluation and follow-up); insufficient supportive and palliative care (lack of platelet transfusions, growth factors, antibiotics, parenteral nutrition, antiemetics, CVCs and parenteral opioids); slow bureaucratic procedures; lack of privacy (promiscuity of sex and age) and hygiene.

Conclusions. In Tanzania, there is an high prevalence of infectious-related, potentially curable cancers, but economical and cultural barriers reduce the possibility of care. At the moment, through a tutorial activity and using the local available tools, the challenges of Associazione Vittorio Tison, IRST, IOR and Istituto Oncologico Veneto (IOV) task force, are to increase oncological and palliative culture and to support the cancer care in Tanzania.

F5* BENEFIT OF PALONOSETRON PLUS SINGLE-DOSE DEXAMETHASONE (DEX) ON DELAYED NAUSEA AND VOMITING DUE TO MODERATELY EMETOGENIC CHEMOTHERAPY (MEC): A POOLED ANALYSIS OF TWO PHASE III TRIALS

Celio L.[1], Bonizzoni E.[2], Bajetta E.[3], Agustoni F.[1], Franceschelli L.[1], Sebastiani S.[4], Perrone T.[5], Aapro M.[6]

[1]Department of Medical Oncology, Fondazione IRCCS, Istituto Nazionale Tumori, Milan, Italy; [2]University Institute of Medical Statistics and Biometry, Milan, Italy; [3]Istituto di Oncologia, Policlinico di Monza, Monza, Italy; [4]Helsinn Healthcare, Lugano, Switzerland; [5]Scientific Department, Italfarmaco, Cinisello Balsamo, Italy; [6]Clinique de Genolier, Genolier, Switzerland

Background. The strongest predictor of delayed chemotherapy-induced nausea and vomiting (CINV) is the occurrence of symptoms during the first 24 hours after chemotherapy. The relationship of acute CINV and delayed CINV was explored using

pooled data from two randomized trials evaluating a DEX-sparing regimen for the prevention of CINV due to MEC.

Methods. A total of 624 chemo-naïve patients with solid tumours undergoing single-day MEC regimens were randomized to receive palonosetron 0.25 mg IV plus DEX 8 mg IV on day 1 of chemotherapy (n = 314) or the same followed by DEX 8 mg orally on days 2 and 3 (n = 310). Patients were categorized by the presence or absence of either acute vomiting (AV) or acute nausea (AN), and the incidence of delayed vomiting (DV) or delayed nausea (DN) was then examined between categories.

Results. Among the 544 patients across both treatment groups with no AV, no DV occurred in 96% (266/278) of patients receiving the 1-day regimen, and in 97% (258/266) of those who received also dexamethasone on days 2 and 3 (Fisher's exact test, p = 0.497). There was no difference also among the 80 patients who did have AV, 23/46 (64%) receiving the 1-day regimen who had no DV while 32/44 (73%) receiving additional DEX doses had no DV (p = 0.470). Of the 390 patients across both treatment groups with no AN, 129/199 (65%) receiving the 1-day regimen and 140/191 (73%) receiving additional DEX doses experienced no DN (p = 0.080). A similar benefit was seen among the 234 patients who did have AN, 21/115 (18%) receiving the 1-day regimen who had no DN while 23/119 (19%) receiving additional DEX doses had no DN (p = 0.868).

Conclusions. Additional DEX doses induced no superior control of delayed CINV in patients with or without acute CINV. This finding supports a pharmacologic effect of palonosetron on delayed symptoms and not simply a persistence of the acute effect of the drug.

F6* RANDOMISED PHASE III CLINICAL TRIAL OF A COMBINED TREATMENT WITH CARNITINE + CELECOXIB ± MEGESTROL ACETATE FOR PATIENTS WITH CANCER-RELATED ANOREXIA/CACHEXIA SYNDROME

Madeddu C., Panzone F., Antoni G., Serpe R., Dessì M., Macciò A., Mantovani G.

Department of Medical Oncology, University of Cagliari, Italy

Background. Cancer-related anorexia/cachexia syndrome (CACS) is a multifactorial syndrome characterized by loss of lean body mass (LBM), metabolic alterations, chronic inflammation and fatigue.

Purpose. A phase III, randomized study was carried out to compare a two-drug combination carnitine + celecoxib ± megestrol acetate for the treatment of cancer-related anorexia/cachexia syndrome (CACS): the primary endpoints were increase of lean body mass (LBM), decrease of resting energy expenditure (REE), decrease of fatigue and improvement of total daily physical activity. Secondary endpoints were: improvement of appetite, quality of life (by the EORTC QLQ-C30), increase of physical performance tested by grip strength and six minute walk test, decrease of ECOG PS and Glasgow Prognostic Score (GPS) and decrease of proinflammatory cytokines.

Patients and methods. Eligible patients were randomly assigned to: arm 1, L-carnitine 4 g/day + celecoxib 300 mg/day or arm 2, L-carnitine 4 g/day + celecoxib 300 mg/day + megestrol acetate 320 mg/day, all orally. All patients received as basic treatment polyphenols 300 mg/day, lipoic acid 300 mg/day, carbocysteine 2.7 g/day, vitamin E, A, C. Treatment duration was 4 months. Planned sample size was 120 patients.

Results. According to the statistical design an interim analysis was planned for futility after the enrolment of 60 patients. The results did not show a significant difference between treatment arms: therefore, the trial was stopped for futility. Analysis of changes from baseline showed that LBM (by dual-energy X-ray absorptiometry and by L3 computed tomography) increased significantly in both arms. REE and fatigue decreased significantly in both arms. Among secondary endpoints, GPS and ECOG PS score decreased significantly in both arms. Physical performance assessed by 6MWT improved significantly in both arms. Toxicity was quite negligible and comparable between arms.

Conclusion. The results of the present study enable us to suggest a simple, feasible, effective and safe, low cost two-drug treatment for CACS including nutraceuticals (i.e., antioxidants): this combination has a favorable cost-benefit profile while achieving optimal patient compliance.

This study was partially funded by AIRC (Associazione Italiana Ricerca per il Cancro), project number 8679.

F7 CLINICAL PREDICTION OF SURVIVAL IN CANCER PATIENTS IN PALLIATIVE HOME CARE SERVICE: EVALUATION OF A SPECIALIST PALLIATIVE CARE TEAM

Rossello R.[1], Grimaldi F.[1], Gambadauro P.[1], Aloi G.[1], Leone A.[1], Salamita G.[1], Germanà A.[1], Micozzi E.[1], Barbera S.[2], Perroni S.[2]

[1]Sisifo Consorzio Cooperative Sociali, Servizio Assistenza Domiciliare Malati Oncologici Terminali, Messina; [2]Dipartimento Cure Primarie U.O. ADI-UVD, Distretto Sanitario di Barcellona PG, ASP 5, Messina

Introduction. The prediction of survival time in patients (pts) with advanced cancer is important both for physicians and pts, to optimize care and improve quality of life. Several researchers have developed prediction models of survival, but these models have several limitations.

The clinical prediction of survival (CPS) is one of the most studied and also subjected to critical review in the literature. To date maintaining its meaning in the prognostic characterization of cancer patients with advanced disease. Its accuracy is limited by the subjectivity of the parameter and the experience of the physician performing the evaluation.

Aims. Purpose of our study was to assess whether the experience acquired over the years by the Unit of Multidimensional Assessment (UMA) of home palliative care service (Sanitary District of Barcellona PG, ASP 5, ME) reported a better prognostic characterization in terms of clinical prediction of survival.

Method. From January 2006 to December 2009, the medical records of the pts included in the service of palliative care home, for terminal cancer pts, were reviewed. In all the pts prior to activate the service was estimated a CPS in order to assign them to a less intensive protocol assistance (A: patients with a life expectancy ≤12 weeks), or more intensive (B: patients with expectation ≤4 weeks of life). The specialist palliative care team was composed of general practitioners, physician specialized in palliative care and physician responsible of the UMA.

Results. 135 patients were evaluated, of which 127 are evaluable for our analysis (8 pts were excluded from the analysis because long survival). Patients characteristics were as follows: median age 72 yrs (range 28.95), gender M/F 74/53, KPS in all pts ≤50. The most frequent tumour sites were: lung (27.5%), gastrointestinal system (27%), urogenital system (20%) and breast (10%). 27.5% of pts were included in the protocol A, and 72.5% in protocol B.

The CPS provided by the specialist palliative care team was in agreement with the actual survival in 66% of pts in 2006, 70% of pts in 2007, 74.4% of pts in 2008 and 73% of pts in 2009.

Conclusion. Our study confirmed that the clinical prediction of survival in expert hands is a good method for the prognostic characterization of cancer patients with advanced illness. The longer experience gained over the years by the evaluation team certainly has a positive effect on the prediction of PCS, doesn't result in a statistically significant difference, this is probably attributable to the small scale of the sample. The use of prognostic score is nevertheless an overcoming of the intrinsic subjectivity of the PCS.

F8 OSTEONCOLOGY TEAM AS MULTIDISCIPLINARY CARE OF PATIENTS WITH BONE METASTASES

Verì A.[1], Vidiri F.[3], Vitale S.[1], Spinelli M.[2], Marcello R.[4], Faiola A.[5], Giordano F.[6], Gasparini G.[1]

[1]Complex Operative Unit of Oncology, [2]Complex Operative Unit of Orthopaedic Surgery, [3]Complex Operative Unit of Radiotherapy, [4]Complex Operative Unit of Radiology, [5]Operative Unit of Neurosurgery of Spinal Column, [6]Operative Unit of Pain Therapy, A.C.O. San Filippo Neri Hospital, Rome

Background. Bone metastases are frequent in cancer patients and they determine serious morbidities. To improve the clinical assessment of the patients with bone metastases at our Center, in June 2009 a multidisciplinary unit of Osteoncology has been activated.

Methods. The team is composed as follows: two oncologists, one specialist in palliative care, one radiotherapist, one orthopedic, one interventional radiologist and one neurosurgeon skilled in spinal diseases. The multidisciplinary medical meeting is held to establish the optimal diagnostic, therapeutic and care pathway with the aim of decreasing waiting times for such category of cancer patients, and, subsequently, of lessening psychophysical suffering. The bimonthly clinic appointment involves three phases: a) the oncologists summarize the clinical case to the whole team; b) all the specialists perform an accurate physical examination of the patient and also investigate the performance status according to the Eastern Cooperative Oncology Group System, and the level of pain according to the Visual Analogue Scale System. All the experts elaborate a clinical report in which are indicated the therapeutic decisions taken for the best treatment of the skeletal pathology; c) the results and therapeutic decisions are debated with the patient and his family.

Results. Fifty-seven patients (13 males, 44 females; median age 61 years [41-91]) have been followed. Reasons for referral to the Center were: diagnostic doubts (30%), first diagnosis (20%), planning of therapeutic program (50%). 120 multidisciplinary consultations have been performed. Sites of primary tumours were breast (60%), prostate (15%), lung (15%), and other tumours (10%). Other results in the following two tables.

Table 1

Features of bone metastases	Patients (%)
Single bone metastases	45
Multiple skeletal metastases	55
Spine only metastases	13
Spine and other bone metastases	52
Only skeletal metastases	64
Visceral and bone metastases	36

Table 2

Main therapeutic decisions	Patients (%)
Radiotherapy	46
Therapy with zometa	26
Percutaneous vertebroplastic or bone biopsy	15
Bone surgery	7
Neurosurgery of the spine	7
Change of therapy with morphine or other opioids	30

Conclusions. Our experience suggests that a multidisciplinary group dedicated to the treatment of bone metastases reduces waiting times, the psychological suffering, and the global time required for medical decisions, finally improving the quality of life of the patients. Present results here discussed offer the possibility to improve bone metastases treatment as recommended by the AIOM guidelines recently published.

F9 DIFFERENT APPROACHES IN THE END OF LIFE CARE IN CANCER PATIENTS IN ONCOLOGY UNIT (OU) VS PALLIATIVE CARE UNIT (PCU). A SINGLE INSTITUTION EXPERIENCE

Cuomo A., Zambelli A., Pagani A., Ponchio L., Da Prada G.A., Fregoni V., Pavesi L., Preti P.

IRCCS Fondazione S. Maugeri, Pavia

Background. Little is known about the end-of-life care (EoL care) in terminally ill cancer patients admitted to different hospital environments. There is concern that terminally ill cancer patients are over treated with chemotherapy, even when such treatment is unlikely to palliate symptoms.

Aim. To compare the use of chemotherapy and other therapeutic approaches in EoL care, according to the OU vs PCU experience.

Patients and methods. In this study we have retrospectively compared the EoL care in the last 30 days of life in 222 consecutive patients admitted to a Palliative Care Unit (PCU n.108) or Oncology Unit (OU n.114) of the same Institution. The patients' characteristics were similar (age 67 ± 11 yrs and 63 ± 9, male/female 53/55 and 56/58, for PCU and OU, respectively) and most of them were affected by lung, breast and colorectal cancer. The admission criteria to a particular unit were not randomized but casual.

Results. The number of diagnostic procedures was evenly distributed among the 2 units and most of the patients underwent at least one routine procedure of chemical examinations. Very few patients had undergone radiotherapy, while palliative chemotherapy was mostly used in the OU (59% vs 9%, $p < 0.001$). Sedation and pain relief therapies were statistically more employed in the PCU (68% vs 8%, $p < 0.0001$ and 83% vs 61%, $p < 0.01$, respec-

tively), as well as psychological support (34% vs 4%, p <0.01) and artificial nutrition (23% vs 8%, p <0.01), while blood transfusion was mostly performed in the OU (16% vs 6%, p <0.05). Only 1 and 5 patients for OU and PCU, respectively, were admitted to a rehabilitation program.

Conclusion. We conclude that the EoL care practice in the last month of life, largely varies even within the same Institution, depending on the type of the hospital units. The PCU seems, at least in our local experience, to guarantee a better pain and uncontrolled symptoms management and psychological support than the OU.

F10 PROPOSAL OF STANDARDS FOR THE OPTIMAL CONTROL OF CANCER PAIN IN ROUTINE PRACTICE AT MEDICAL ONCOLOGY UNITS: PAIN MONITOR PROJECT

Melotti B.*, Cricca A.*, Rocchi G.*, Mattei M.§, Baroncini M.°, Galli S.°, Mirante M.°, Martoni A.*

**Medical Oncology Unit, §Radiotherapy Unit, °Hematology Unit, S. Orsola-Malpighi Hospital, Bologna, Italy*

Background. Cancer pain is often underestimated and undertreated. The aim of achieving optimal pain control in each cancer patient requires an accurate knowledge of etiopathology, intensity and modifications.

Materials and methods. Within the Pain-Free Hospital project at Sant'Orsola-Malpighi Hospital in Bologna, the twice daily pain measurement (by VAS first and then by NRS) was introduced in 2003 in all the patients admitted to the inpatient wards of the Onco-Hematologic Department. A training course addressed to the whole nursing and medical staff was started and is repeated on yearly basis.

As a development of this experience, since 2007, under the PAIN MONITOR project, we identified some efficiency and effectiveness indicators of the process that is responsible for optimal control of cancer pain. The more representative indicators were as follows: 1) No. of NRS records collected/no. of pain recordings to be collected throughout the hospitalization (twice daily); 2) no. of times the doctor started or changed the treatment/no. of times when there was an increase by at least 2-point NRS for at least two consecutive evaluations (applies only to values of NRS ≥3); 3) no. of times the doctor started or changed the treatment/no. of times that there were two or more interventions for back through pain within 24 hours; 4) no. of pts discharged with NRS less than one at entry/no. of pts with NRS >3 at entry.

Results. In 2010 the results based on 2 semester-long audits were as follows (by indicator): no. 1: 97%, no. 2: 64%, no. 3: 70%, no. 4: 83%. With the activation of this project a growth in the consumption of strong opioids and paracetamol and a reduction in NSAID consumption was registered by Hospital Pharmacy.

Conclusions. This project has defined indicators of efficacy and effectiveness in the pain control process. The proposed standard levels need to be corroborated in a multicenter study.

F11 IMPACT OF WORRY ON PSYCHO-PHYSICAL SYMPTOMS IN HOME-CARED CANCER PATIENTS FAMILY CAREGIVERS

Zavagli V.[a], Varani S.[b], Samolsky-Dekel A.R.[b], Brighetti G.[a], Pannuti F.[b]

[a]Department of Psychology, University of Bologna, Bologna, Italy; [b]ANT Italia Foundation, Bologna, Italy

Background. Cancer patients family caregivers are exposed to several physical and emotional distress. Many recent reviews have provided strong evidence linking negative affective states and dispositions to disease and bad health. Moreover, recent studies suggested that perseverative cognition, as manifested in worry, plays a role in anxiety disorders and it is a crucial factor in somatic health. The present study focused on physical symptoms of cancer family caregivers. In particular, it was designed to clarify if worry might act directly on psychological and somatic diseases. The study has been developed by ANT Italia Foundation at an oncological hospital at home in Bologna.

Method. The sample consists of 107 family caregivers (77 female and 30 male). Participants completed a battery of self-report questionnaires including the Caregiver Burden Inventory, the Penn State Worry Questionnaire, the Psycho-Physiological Inventory and the Beck Depression Inventory. Subjects underwent tests twice: at the moment of oncological home-care request and after three weeks.

Results. Worry level resulted high among informal caregivers (1st evaluation: mean = 42.87; Sd = 11.78; 2nd evaluation: mean = 43.35; Sd = 13.64) and resulted also as a stable trait over time. Significant results have been found in the relationship between psychological health and somatic symptoms of caregivers. Particularly it has been highlighted a significant positive correlation between worry level and caregiving burden and somatic symptoms. Moreover, worry resulted as a powerful and solid predictor of physical symptomatology (r = 0.5; p = 0.000001). Lastly, high worry levels resulted positively correlated to high depression levels (r = 0.46; p <0.000001).

Conclusions. The results show that worry is a crucial variable for the wellbeing of family caregivers involved in such a difficult task as cancer patient's assistance. In fact, worry determines important consequences in terms of psychophysical symptomatology. It may become a direct threat to both mental and physical health, making patients assistance even more difficult. These results have great practical and operative value. In fact cancer patients health is deeply correlated to family caregiver wellbeing.

F12 GRANULOCYTE COLONY-STIMULATING FACTORS (G-CSF) USE IN CLINICAL PRACTICE: POLO NORD REGISTRY-BASED COHORT STUDY

Fagnani D.[1], Isa L.[2], Verga M.[1], Nova P.[1], Casartelli C.[3], Filipazzi V.[4], Danova M.[5], Farina G.[6], Pugliese P.[7], Fava S.[8], Bertolini A.[9], Cimminiello C.[1], Boracchi P.[10], Marano G.[10], Panzarino C.[1] on behalf of Polo Nord Group

[1]A.O. di Desio e Vimercate; [2]Ospedale di Gorgonzola; [3]Ospedale Valduce, Como; [4]Ospedale Sacco, Milano; [5]IRCCS Policlinico S. Matteo, Pavia; [6]Ospedale Fatebenefratelli e Oftalmico, Milano; [7]Ospedale S. Anna, Como; [8]Ospedale Civile di Legnano; [9]Ospedale di Sondrio; [10]INT, Milano

Background. G-CSFs are widely used to reduce myelotoxicity of chemotherapy (Th) and to allow its regular administration. National and International Guidelines (GU) recommend their use. The aim of the study is to evaluate G-CSF, pegfilgrastim (PEG) and filgrastim/lenograstim (FL), patterns of use in clinical practice (CP), comparing their adherence to AIOM (Medical Oncology Italian Association) GU, effectiveness and tolerability.

Materials and methods. Data from 622 consecutive patients (pts), receiving G-CSF for the first time during a line of Th, were enrolled from 09/2008 to 11/2010, in 10 Lombardy Italian cancer centers. Data recorded by 2882 follow-up (FU), corresponding to Th cycles: age, neoplastic disease and stage, Th regimens, febrile neutropenia risk (high or low) according to pts risk factors, blood counts, kind of G-CSF and patterns of use, febrile neutropenia (FN), G3-4 neutropenia, hospitalization due to infections (HDI), dose reduction (DR), Th delay (ThD) and bone pain.

Results. Mainly G-CSF supported neoplastic diseases (622 pts): breast cancer (B) 229 (37%), lung cancer (L) 102 (16%) and lymphomas (LY) 71 (11%), but with different use modality: B ≥ main use in adjuvant therapy (141; 62%), to guarantee dose intensity in pts at low risk of FN (137; 60%); L/LY (102/71 pts) ≥ main use in advanced disease (L90%, LY100%), to support pts at high risk of FN (L72%, LY69%).

		PEG	FL	p
Patterns of use	1st prophylaxis (FU)	43% (313/722)	57% (409/722)	
	2nd prophylaxis (FU)	14% (191/1340)	86% (1149/1340)	
	Therapeutic use (FU)	/	100% (356)	
Adherence to GU	1st prophylaxis (pts)	75% (64/85)	55% (53/97)	0.006
	2nd prophylaxis (pts)	16% (10/64)	25% (78/313)	NS
		59%* (38/64)	63%* (197/313)	NS
	Timing start (FU)	99% (501/504)	62% (972/1558)	<0.00001
Effectiveness (FU)	FN rate	1.6% (8/504)	0.7% (11/1558)	NS
	G3-4 Neutropenia rate	6% (30/504)	7% (110/1558)	NS
	HDI	1% (5/504)	0.25% (4/1558)	NS
	DR	1.6% (8/504)	4.1% (64/1558)	NS
	ThD	2.6% (13/504)	5% (77/1558)	NS
Side effects	Bone pain (FU)	7.3% (37/504)	5.7% (109/1914)	NS

* Including pts at high risk of FN according to pts risk factors.

Conclusions. Results suggest the high G-CSFs effectiveness and tolerability in CP, where their use is extended beyond GU recommendations to support pts at high risk of FN and to guarantee dose intensity. The use of PEG as primary prophylaxis and timing start fits to GU more than FL, but no significant difference was found in terms of effectiveness and tolerability.

F13 MONITORING THERAPEUTIC USE (TU) APPROVALS OF ONCOLOGY DRUGS ESTABLISHED UNDER MINISTERIAL DECREE 05/08/2003 AS ISSUED BY THE ETHICS COMMITTEE OF THE AREA VASTA ROMAGNA AND IRST (CEAV/IRST) FROM JULY 2007 TO AUGUST 2010

Donati C.[1], Burioli P.[1], De Giorgi U.[2], Caruso F.[3], Maretti S.[4], Plescia A.[5], Rizzi N.[1], Minguzzi M.[1], Cascinu S.[6]

[1]Oncological Pharmacy, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), Meldola, Italy; [2]Oncological Division IRST; [3]Pharmacy, Cesena Health Authority; [4]Oncological Pharmacy, Ravenna Health Authority; [5]Pharmacy, Rimini Health Authority, [6]Oncological Division, Ancona

Purpose. The Ethics Committee of the Area Vasta Romagna (AVR) and the Cancer Institute of Romagna (CEAV/IRST) is based at IRST and is supported by a technical and scientific secretariat that serves all the local Health Authorities in the Romagna region.

Materials and methods. All information pertaining to the therapeutic use (TU) of drugs is derived from a custom database set up by the CEAV/IRST secretariat that is linked to another database that manages all cancer treatments in the AVR (developed by Log80-IRST). For each patient, it is possible to link TU with up-to-date data on the lines of therapy, the number of cycles administered, outcomes, health authority costs, and indications for future drug registrations.

Results. During the course of the study, a total of 18 drugs have been approved for therapeutic use, 12 for the treatment of oncological diseases, and 6 for non-oncological diseases. Overall, 206 patients were treated, with an average of 16.5 and 1.5 patients for each cancer- and non-cancer drug, respectively. The report highlighted the fact that: 1) in reality, many of the patients assigned to TU did not actually start treatment; 2) the average monthly treatment rate for the different drugs varied significantly; and 3) there was great variability in the duration of treatment among patients assigned to the same drug, particularly for gefitinib, everolimus and ipilimumab. We were able to provide treatment to many patients even though the drugs were not yet widely available in the market, without incurring any increased expenditure for local Health Authorities. The estimated cost of simulated TU according to the drug registration price was about 1.7 million Euros.

Conclusion. Our work has improved the way in which we redefine the TU approval procedure, focusing attention on clinical response factors that could support clinical practice, especially if compared with data from other settings.

F14 PALLIATIVE TREATMENT OF PERITONEAL CARCINOMATOSIS: THE ROLE OF HIPEC (INTRAPERITONEAL HYPERTHERMIC CHEMOTHERAPY) IN A SINGLE CENTER EXPERIENCE

Astara G.*, Orgiano L.*, Manca A.**, Marini S.***, Mantovani G.*

**Department of Medical Oncology I, **Department of General Surgery G, ***Department of Radiology, Azienda Ospedaliero-Universitaria, Cagliari*

Aim. The aim of the study was to evaluate the role of HIPEC (intraperitoneal hyperthermic chemotherapy) in the palliative treatment of peritoneal carcinomatosis from advanced cancer of different origin.

Patients and methods. Twenty patients with intraperitoneal carcinomatosis were treated with HIPEC from May 2006 to April 2011. Five males and fifteen females between 54 and 85 years. Malignant ascites was from ovarian cancer (10 cases), pancreas

(3 cases), cervical cancer (2 cases), gastric cancer (2 cases), colorectal cancer (1 case), mesothelioma (1 case) and unknown primitive cancer (1 case). HIPEC used cisplatin, mytomicin or paclitaxel based on the different type of primary tumour for 60' at about 41 °C intra-abdominal temperature. Main endpoints: the increase of free interval between 2 drains, the progressive reduction of ascites and the improvement of quality of life evaluated with the ECOG-PS and the questionnaire EORTC QLQC30.

Results. Three patients "lost" at the follow-up, while seventeen were completely evaluable. The treatment was well tolerated: 12 patients had nausea of grade I, 2 had vomiting of grade I and 4 had vomiting of grade II, 1 patient had neutropenia of grade III, 8 patients had abdominal pain and 2 had peritonitis from chemotherapy. The median free interval between drains passed from 1 every 9.8 days to 1 every 38.6 days. The features of ascites passed from hemorrhagic to blood serum-like. The median volume drained passed from7.2 L to 1.1 L. The median abdominal circumference passed from 105.3 cm to 101.2 cm. Nine patients had improved their PS, 5 had the same one before and after the treatment, 3 had worsened it. Every patients had improved their personal score with the EORTC QLQC-30.

Conclusions. At present only 3 patients are still alive and they enjoy good PS and QL whilst 14 died for complications of cancer.

F15 EFFECTS OF ZOLEDRONIC ACID ON SIGNIFICANT BIOMARKERS OF PATIENTS WITH BONE METASTASES FROM ADVANCED STAGE CANCER: A PHASE IV STUDY

Puzzoni M., Astara G., Madeddu C., Panzone F., Spano L., Antoni G., Tanca F.M., Mantovani G.

Department of Medical Oncology, University of Cagliari, Italy

Background. Zoledronic acid (ZA) is a highly-effective additional treatment approach for cancer patients with bone metastases. Recent evidence shows that ZA may also have antineoplastic effects.

Aim. The aim of the present study was to assess ZA activity in the prevention/reduction of skeletal-related events (SREs) in cancer patients with bone metastases and assess the role of N-telopeptide of type I collagen (NTX) as prognostic and even more predictive factor/surrogate marker of efficacy. Moreover, we investigated the ZA effect on cytokine levels (IL-1,6,8; TNFα), inflammation-related (C-reactive protein, CRP) and lipid metabolism (cholesterol and triglycerides) indices.

Patients and methods. The study was an observational retrospective phase IV study. Thirty-three advanced cancer patients (M/F: 16/17, mean age 68 years) with bone metastases were enrolled. They were treated with ZA 4 mg q4w from April 2005 to July 2010 with a mean of 42 administrations per patient. The changes of laboratory parameters levels before and after ZA therapy were assessed by two-sided Student's t test and a $p \leq 0.05$ was considered statistically significant. Toxicity was assessed by the National Cancer Institute Common Toxicity Criteria (NCI-CTC-V_3). The only criterion for bone disease progression was the appearance of new bone lesions.

Results. We observed 6 SREs (mean time to first SRE 34±16.86 months). As for laboratory parameters IL-8 and PCR decreased at months 6 and 12, TNFα and triglycerides decreased at month 12; NTX decrease was not statistically significant. As for severe adverse events, 1 ONJ occurred.

Conclusions. ZA was able to prevent/reduce SREs in cancer patients with bone metastases; the downregulation by ZA of serum levels of IL-8, TNFα and PCR seems to suggest that this is a probable mechanism of action by which ZA exerts its clinical effect. The trend toward a decrease of NTX warrants further investigation.

This study was partially funded by AIRC (Associazione Italiana Ricerca per il Cancro), project number 8679.

F16 PREVENTION OF JAW'S OSTEONECROSIS (ONJ) IN CANCER PATIENTS TREATED WITH BISPHOSPHONATES: A MONOINSTITUTIONAL EXPERIENCE

Piazza E.*, Sparaco A.°, Bianco R.^, Ghezzi M.°, Donati G.°, Montebello A.°, Andriella K.°, Rania V.°, Filipazzi V.*, Cattaneo M.T.*, De Troia B.*, Isabella L.*, Ferrario S.*, Gambaro A.*

**Oncology, °Odontology, ^Radiology Department, "Luigi Sacco" Hospital, Milan*

Background. Bone metastases are a major cause of morbidity in cancer patients. Their treatment includes bisphosphonates (BP), which are associated with avascular osteonecrosis of the jaw (ONJ). BP have been also used for a long time in treatment of osteoporosis. It is important to evaluate the cases individually, taking into account general health and, in particular, the condition of the oral cavity. Our aim was to evaluate the efficacy of a prophylactic management protocol to prevent ONJ and describe the few cases recorded.

Patients and methods. All patients with bone metastases treated in our department with i.v. bisphosphonates went to dentist evaluation for dental check-up within a multidisciplinary protocol designed in collaboration with Odontology Department of our hospital. It recommends orthopantomography, dental and parodontal treatments for oral healthy before starting BP every 6 months.

Results. We have not observed any case of ONJ since this preventive oral protocol was activated in January 2011. The 6 ONJ cases were observed in pts treated before that date. They were 4 F + 2 M, median age 66 years (range 40-78), 5 cancer pts (1 NSCLC +1 breast cancer + 2 multiple myeloma +1 NHL) treated with i.v. zoledronic acid, while in one case ONJ developed in an osteoporotic old female treated with intramuscular clodronic acid for 2 years. In three cases the BP treatment was concomitant with chemotherapy, 1 with endocrine treatment and 1 with radiotherapy. The time from start of BP therapy to ONJ diagnosis was between 2 to 24 months. Forty-five patients have been recruited to date and we have not recorded any new case of ONJ, nevertheless they received dental evulsion, tartarus clear out, endodental care or dental plate.

Conclusions. Our results show that ONJ can appear also few months after the start of BP treatment. Surgical approach can be used in suitable cases. It is still too early to understand whether activation of the specific oral protocol will lead to a decrease in ONJ. Closer cooperation is needed among specialists to define guidelines for the prevention of ONJ in patients with bone metastases[1]. Monitoring is going on.

References

1. Ruggiero S et al: Practical guidelines for the prevention, diagnosis and treatment of ONJ in patient with cancer. J Oncol Pract, 2 (1): 7-14, 2006.

F17 EXPERIMENTAL PERSPECTIVE, COGNITIVE STUDY OF PERCEPTION EVALUATION OF FATIGUE AND DEPRESSION AMONG CAREGIVERS, ONCOLOGICAL PATIENTS IN CHEMOTHERAPY (NEOADJUVANT, ADJUVANT AND ADVANCED) AND ONCOLOGIST TEAM. EQUI-CAR 09 STUDY

Barzelloni M.L., Stanzione C., Carnicelli P., Izzo R.

Diagnosis and Oncology Treatment Center "G. da Procida" Hospital, Salerno

The EQUI-CAR 09 is an observational study, this study uses the FACIT-F questionnaire for evaluation of fatigue and the ZUNG self-evaluation scale for depression. The study was carried out between 01/09 and 12/09, and it recruited 60 patients and 60 caregivers. The study was carried out on patients with lung, breast and colon cancer, that needed chemotherapy and family members chosen as caregivers. The objective was to evaluate the agreement of fatigue perception and depression of caregivers, oncological patients in chemotherapy and oncological team. Patients, caregivers and doctors filled in FACIT-F and ZUNG questionnaires at the baseline after two cycles of chemotherapy, after four at the end of the treatment. The evaluation of the ZUNG and FACIT-F, on patients in neoadjuvant and adjuvant treatment has highlighted high levels of fatigue and depression, in advanced patients the levels were less high. The evaluation of the ZUNG and FACIT-F on caregivers, with patients in neoadjuvant and advanced stage, showed high levels of fatigue and depression, whereas patients in adjuvant treatment showed lower levels of fatigue and depression. The evaluation of the three oncologists (average age 52.6) has highlighted low levels of fatigue and depression. The study EQUI-Car 09 draws attention to the necessity of providing the oncological patients and caregivers also with preventive psychological backing. The team has not showed burnout, that is very common in the helping profession, due to the weekly psychological aid related to the team work problems, and to the team psycho-oncological experience.

F18 PSYCHOLOGICAL NEEDS AND UNDERLYING REQUESTS. THE CHALLENGE OF THE MEDICAL TEAMWORK IN CARING FOR PATIENTS WITH CANCER

Ucci G., Solari F., Zanaletti F., Burgazzi A., Costa G., Pozzoli R., Carenzi M.R., Montanari G., Tansini G.

Dipartimento Oncologico, Azienda Ospedaliera della Provincia di Lodi

The literature on the psychological distress in patients with cancer recommends that the whole medical teamwork has to take into account and manage the underlying requests of patients during their illness experience. For this reason, the present research aims to explore the underlying requests of patients with cancer, avoiding communicative misunderstanding, and supporting them.

The research design includes 230 cancer patients starting the oncological-adjuvant treatments (between the 1st and the 2nd session of chemotherapy) in the last 2 years.

Distress and psychological needs were assessed using the Psychological Distress Inventory (PDI) and the Needs Evaluation Questionnaire (NEQ). The categorical measures were analyzed running two statistics: Chi Square test and Hierarchical Log Linear Model (HILOG).

Data from PDI show that patients starting a chemotherapy treatment do not clearly express any psychological intervention (75%). The most representative psychological needs are: information on prognosis (53%) and information on medical exams (30.5%).

Factor analysis on NEQ outcomes data shows 6-cluster where emotional support is the most expressed need (83%). Furthermore, cancer patients with low level of distress show a statistically significant interaction between the needs of information about diagnosis and prognosis, and sincere and clear communication with the oncologist. On the other hand, cancer patients with high distress level show a significant interaction between the needs of support, and sharing the illness.

Cognitive and emotional skills of patients with cancer starting an oncological treatment and facing a new traumatic pathway are primarily focused on the resolution and management of health-related stress. Psychological needs seem to be on the background, and hided into more informative and practical requests. Outcomes show that the supporting and sharing requests of cancer patients are oriented not only to the family network, but also to the medical teamwork; for this reason the medical teamwork is the first buffer helping patients in coping with stress, digging up the hided and underlying psychological needs.

F19 ACUTE CARDIAC TAMPONADE (CT) SECONDARY TO MALIGNANT PERICARDIAL EFFUSION (MPE) IN BREAST AND LUNG CANCER: THE BENEFIT OF INTRAPERICARDIAL INSTILLATION OF BLEOMYCIN

Occelli M.[1], Cristofano A.[2], Silvestris N.[3], Trogu A.[2], Mozzicafreddo A.[2], Procaccio L.[2], Fea E.[1], Denaro N.[1], Merlano M.[1], Numico G.[2]

[1]Oncologia Medica, Ospedale S. Croce e Carle, Cuneo; [2]Oncologia Medica, Ospedale U. Parini, Aosta; [3]Oncologia Sperimentale e Clinica, Istituto Giovanni Paolo II, Bari

Introduction. MPE is the most frequent manifestation of malignant involvement of the heart; it is often asymptomatic and not recognized until CT develops. If not promptly treated, tamponade can produce acute life-threatening cardiovascular collapse. We evaluated the short-term safety and the long-term benefit of pericardiocentesis in association with intrapericardial instillation of bleomycin in advanced lung and breast cancer pts with CT.

Materials. CT secondary to MPE was diagnosed in 15 consecutive pts (11 with lung and 4 with breast cancer) by CT scan and echocardiography. Chemotherapy was still ongoing in 7 patients. Cytologic examination was performed in all patients. Pericardiocentesis was followed by 1 or 2 intrapericardial administrations of bleomycin 10 mg along with lydocaine 100 mg. Treatment toxicity was evaluated during and after the hospitalization period. Effusion response rate and relapse were evaluated by follow-up CT scan and echocardiography.

Results. All patients had a prompt symptom relief and 9 of them (60%) had no side effects while the others had few and rapidly controlled side effects, consisting in thoracic pain (4),

fever (7%), fainting (12%) and supraventricular arrhythmia, (one case, related to myocardial malignant infiltration). All patients had a response to the treatment and 53% experienced a complete response. Only one patient had an effusion relapse (after 6 months) and was effectively treated with surgical pleuro-pericardial window. Overall, median survival was 40.6 weeks and 1-year survival was 47.9%. In pts with breast cancer median survival was 81.3 weeks while was 6.0 weeks in lung cancer patients.

Conclusions. Although pericardiocentesis effectively relieves symptoms and improves hemodynamics, fluid reaccumulates in as many as 60% of cases. Pericardial sclerosis with bleomycin is useful to prevent relapse, is related to few side effects and does not prolong hospitalization. Simple pericardiocentesis may be appropriate for pts with short life expectancy. Instead pts with longer prognoses will likely benefit most from bleomycin administration.

F20 MALNUTRITION EVALUATION AND THERAPY IN THE ONCOLOGICAL OUTPATIENTS' CLINIC SETTING

Pegoraro M.C.[1], Schiavo J.[2], Magazù M.[1], Forni C.[1], Padovani M.[1], Binato S.[1], Barana D.[1], Ronzani G.[2], Oliani C.[1]

[1]UOC Oncologia, [2]UOSD Dietetica e Nutrizione Clinica, ULSS5 Ovest Vicentino

Malnutrition is prevalent in cancer patients, especially those with solid tumours. Poor nutritional status can result in decreased quality of life, functional status, and response to therapy. Malnutrition in cancer has been mainly evaluated in the advanced phases of the disease and in hospitalized patients (pts). Our study is meant to investigate the nutritional status in an oncological outpatients' clinical setting. In December 2009 our Oncological Unit and the Clinical Nutrition Unit began the malnutrition screening of patients at first oncological visit. Patients are evaluated by means of the Malnutrition Universal Screening Tool (MUST) comprising the BMI (Body Mass Index), the percentage of weight loss and a measure of the reduced food intake. If the score obtained is ≥2 the patient successively undergoes a specific nutritional evaluation, including serum biochemistry (e.g. inflammatory markers and serum albumin), impedentiometry and handgrip. Furthermore a personalized nutritional therapy is proposed (increase of the daily dietary intake, dietary supplements, artificial nutrition). In the 230 MUST evaluations analyzed up to now 138 (60%) pts resulted at null risk, 37 (16%) corresponded to a moderate risk (MUST score 1) and 55 (24%) to a high risk (MUST score ≥2). Of the high risk category 29 pts (52.7%) had a gastroenteric cancer. In these pts, the median percentage of weight loss has resulted to be 11.9 ± 10.4% and the median BMI 20.8 ± 3.8 kg/m^2. The MUST score ≥2 has been determined by a loss weight >10% in 38 pts (69%), by a BMI <8.5 kg/m^2 in 11 pts (20%) and by both these parameters in 2 pts (3.7%); four patients (7.3%) fell into the high risk score for the reduced food intake >50%. In our preliminary data BMI doesn't seem to be a useful parameter by itself in order to identify the malnutrition risk while the percentage of weight loss resulted more specific.

F21 EXPERIMENTAL PROSPECTIVE COGNITIVE STUDY OF EVALUATION OF THE CONCORDANCE OF FATIGUE AND DEPRESSION PERCEPTION AMONG CAREGIVERS, AND TEAM TREATING CANCER PATIENTS RECEIVING CHEMOTHERAPY IN PATIENTS WITH ORAL THERAPIES TO SYSTEMIC THERAPIES. EQUI-CAR 10 STUDY

Carnicelli P., Mogavero A., Stanzione C., Izzo R., Barzelloni M.L.

Diagnosis and Oncology treatment Center, "G. da Procida" Hospital, Salerno

The EQUI-CAR 10 is a spontaneous, observational study which uses the FACIT-F questionnaire for evaluation of fatigue and the ZUNG self-evaluation scale for depression. The study was carried out between 01/10 and 12/10, and it recruited 60 patients and 60 caregivers. The study was carried out on patients with lung, breast and colon cancer, that needed chemotherapy and family members were chosen as caregivers. The objective was to evaluate the agreement of fatigue perception and depression of caregivers, oncological team and oncological patients in oral chemotherapy to intravenous therapy. Patients, caregivers and doctors filled in FACIT-F and ZUNG questionnaires at the baseline after three cycles of chemotherapy, after six at the end of the treatment. The evaluation of the ZUNG and FACIT-F, on patients treated whit intravenous therapy showed levels of fatigue and depression significantly higher, lower than the levels in patients treated with oral therapy, even when treated for advanced disease. The evaluation of the ZUNG and FACIT-F on caregivers of patients treated whit therapies systemically administered showed levels of fatigue and depression significantly elevated; levels are lower for patients treated with oral therapies, even when treated for advanced disease. The evaluation of the ZUNG and FACIT-F of three oncologists (average age 52.6) has highlighted low levels of fatigue and depression, for both types of patients, slightly more significant for patients with systemic therapy related to the management of side effects. The study results showed that cancer patients and caregivers have high levels of fatigue and depression both related to the stage of disease (results obtained with the study EQUI-CAR 09), and to the mode of administration of the drug. According to what has been said previously, it is necessary to provide cancer patients and caregivers with appropriate programs and psychological and preventive support.

F22 A MAKE-UP PROGRAM FOR WOMEN DIAGNOSED WITH CANCER: A WALCE (WOMEN AGAINST LUNG CANCER IN EUROPE) COLLABORATION WITH "LA FORZA E IL SORRISO, L.G.F.B. ITALIA"

Demichelis S., Vavalà T., Vallone S., Longo M., Rapetti S.G., Capelletto E., Rovere G., Novello S.

University of Turin, AOU San Luigi, Orbassano (TO)

Background. The Look Good... Feel Better® is a worldwide free make-up workshop program for women diagnosed with cancer and who are undergoing chemotherapy, radiotherapy or other cancer treatments. The program is carried out in local hospitals and it offers free beauty workshops which are strictly non-medical; the aim is to help women to regain self-confidence, improving quality of life and appearances by using beauty techniques. The Look Good... Feel Better® program is currently active in 22 countries worldwide and in 2006 arrived in Italy as "La forza e il sorriso – L.G.F.B. Italia". WALCE Association began its collaboration with La forza e il sorriso – L.G.F.B. Italia in 2009.

Methods. From March 2009 to December 2010, WALCE have organised 34 make-up workshops of "La forza e il sorriso – L.G.F.B. Italia" at the San Luigi Hospital (Orbassano, Turin, Italy) in collaboration with 5 local cancer centers and institutes. 248 ladies attended the free make-up workshops, guided by 7 voluntary beauticians and with support of a psycho-oncologist. 6% had a diagnosis of lung cancer and the majority was aged 50-60 yrs. Everyone filled-in an anonymous beauty-workshop evaluation questionnaire.

Results. 63% were enthusiastic, while 37% were greatly satisfied with the results. 98% declared to have learnt useful advice whereas 2% were a little doubtful. However, the overall response was most positive. Adjectives used to describe patients feelings at the end of the workshop were: beautiful, happy, more positive, prettier and attractive. From the survey, 86% of the ladies had forgotten about the illness during the moment they attended the event. It was expressed by an overall 78% as being a positive experience meeting other ladies in similar situations.

Conclusions. The sense of wellbeing shared in a relaxed atmosphere amongst other ladies who have the same anxieties has proven to be an incentive to fight against cancer. In next workshops a more detailed evaluation of psychological aspects of patients' interpersonal relationships and the impact on disease outcomes will be planned.

F23 TRANSMUCOSAL FENTANYL (TF) AND BREAKTHROUGH PAIN (BP): POOLED ANALYSIS OF RANDOMIZED CLINICAL TRIALS (RCTS)

Tamburini E., Tassinari D., Gianni L., Pittureri C.[1], Maltoni M.[2], Poggi B., Arcangeli V., Papi M., Drudi F., Pasini G., Fantini M., Ravaioli A.

Oncology Department, Infermi Hospital, Rimini, Italy; [1]Unit of Palliative Care-Hospice, Savignano sul Rubicone, Cesena, Italy; [2]Palliative Care Unit, IRST, Meldola, Italy

Background. Transmucosal fentanyl probably represents the standard of care in the treatment of BP; nevertheless, immediate-release morphine has large use in clinical practice. The aim of our review was to analyze the use of TF in the control of BP, exploring the possibility of detecting some applications in clinical practice.

Methods. MEDLINE, EMBASE and Cochrane Systematic reviews databases from January 1966 to May 2011 were searched independently by two Authors (E. Tamburini and D. Tassinari). A systematic review of the main oncologic and palliative congress reports of the period 2000-2010 was performed by the same Authors. All randomized phase III trials comparing TF with placebo or other approaches in treatment of BP were considered eligible and included in the selection. Primary endpoint was pain intensity difference at 15 minutes (PID15). Secondary endpoints were pain intensity difference at 30 minutes (PID 30), and pain intensity difference at 5 minutes (PID 5). Heterogeneity between the trials was assessed using the Mantel-Haenszel test. An alpha error <5% was assumed as index of statistical significance.

Results. 835 patients in 10 trials were randomized to placebo or TF in the treatment of BP. 468 patients in 6 trials were randomized to TF or other approaches. PID 15 ($p < 0.0001$, difference in means 0.6) and PID 30 ($p < 0.0001$, difference in means 1.033) significantly improve in patients treated with TF when compared with placebo.

Conclusions. TF significantly improves PID 15 and PID 30 when compared with placebo. However literature data appears inconclusive on the role of immediate-release morphine compared with TF and on the effectiveness of different formulations of TF. Further trials are still necessary to better define the role of TF in the treatment of BP.

F24 INTEGRATION OF THERAPY WITH BONE-SEEKING RADIONUCLIDES IN A MULTIDISCIPLINARY APPROACH TO TREAT PATIENTS WITH PAINFUL BONE METASTASES

Mariani G.[1], Bernardo G.[2], Bordonaro R.[3], Condemi G.[4], Mantini G.[5], Mazzarotto R.[6], Monari F.[7], Salvatori M.[8], Sciuto R.[9]

[1]Regional Center of Nuclear Medicine, University of Pisa Medical School, Pisa, Italy; [2]Medical Oncology, "Salvatore Maugeri" Foundation, Pavia, Italy; [3]Medical Oncology, "Garibaldi" Hospital, Catania, Italy; [4]Medical Oncology, Town Hospital, Reggio Calabria, Italy; [5]Radiation Oncology, Catholic University, Rome, Italy; [6]Radiation Oncology, "S. Orsola-Malpighi" University Hospital, Bologna, Italy; [7]Radiation Oncology, "Bellaria" Hospital, Bologna, Italy; [8]Nuclear Medicine, Catholic University, Rome, Italy; [9]Nuclear Medicine, "Regina Elena" National Cancer Institute, Rome, Italy

Palliative therapy of pain from osteoblastic bone metastases with bone-seeking radiopharmaceuticals has proven effective since at least three decades. Nevertheless, this therapy, which is feasible and safe even with repeated treatments, is still largely underutilized. There are no obvious reasons for such underutilization, considering that these agents (especially those with shorter physical half-life) have a quite favourable toxicity profile (despite diffuse prejudice on possible myelotoxicity), can be administered on an outpatient basis with minimum discomfort to patients, and radiation protection requirements can easily be implemented. Furthermore, this therapy is often deferred as much as possible and employed as a last resort, based on the fear that bone-seeking radiopharmaceuticals might adversely affect the efficacy of other therapies. Whereas, growing clinical evidence supports the concept that benefits from this therapy are greatest when employed earlier during the course of metastatic disease to bone. Furthermore, ongoing clinical trials disclose promising results concerning synergistic effects of bone-seeking agents with other forms of therapy (such as medical therapies and external beam radiation therapy), with possible anti-tumour efficacy beyond simple palliation of bone pain.

A panel of experts designated by the Italian Association of Nuclear Medicine (AIMN), the Italian Association of Medical Oncology (AIOM) and the Italian Association of Radiation Oncology (AIRO) was convened to define by consensus (based on analysis of published literature) general recommendations concerning optimal integration of therapy with bone-seeking radiopharmaceuticals in a multidisciplinary approach to treat patients with painful bone metastases. The panel has identified the clinical conditions where integration of this form of therapy with other treatments (chemotherapy and/or external beam radiation therapy among others) is feasible and potentially leading not only to improved quality of life but also to better progression-free and overall survival of patients. A reasoned algorithm has thus been developed to optimize both in the short term and in the long term integration of therapies available for patients with metastatic disease predominantly affecting the skeleton.

F25 PRELIMINARY RESULTS OF AIOM LOMBARDIA SURVEY ON TREATMENT OF CHEMOTHERAPY INDUCED ANEMIA (CIA)

Cortinovis D.[1], Beretta G.[2], Piazza E.[3], Luchena G.[4], Aglione S.[5], Bertolini A.[6], Buzzoni R.[7], Cabiddu M.[8], Carnaghi C.[9], Danova M.[10], Farina G.[11], Ferrari V.[12], Frascaroli M.[13], Reni M.[14], Tansini G.[15] on behalf of AIOM Lombardia

[1]UO Oncologia Medica, H S Gerardo, Monza; [2]UO Oncologia Medica, Humanitas Gavazzeni, Bergamo; [3]UO Oncologia Medica, H L Sacco, Milano; [4]UO Oncologia Medica, H S Anna, Como; [5]UO Oncologia Medica, H Vimercate (MB); [6]UO Oncologia Medica, H Civile, Sondrio; [7]UO Oncologia Medica, Istituto per la Cura dei Tumori, Milano; [8]UO Oncologia Medica, H Treviglio-Caravaggio (BG); [9]UO Oncologia Medica, Humanitas Mater Domini, Castellanza (VA) e UO Oncologia Medica ed Ematologia, Istituto Clinico Humanitas, Rozzzano (MI); [10]UO Oncologia Medica,Ospedale Civile, Vigevano (PV); [11]UO Oncologia Medica, H Fatebenefratelli, Milano; [12]UO Oncologia Medica, Spedali Civili, Brescia; [13]UO Oncologia Medica, Fondazione S Maugeri, Pavia; [14]UO Oncologia Medica, IRCCS Istituto Scientifico S Raffaele, Milano; [15]UO Oncologia Medica, H Lodi

Background. Anaemia prevalence and incidence in chemotherapy treated patients is high. Erithropoietic stimulating agents (ESAs) are generally employed in CIA management. However, other treatments such as red blood transfusion or iron supplementation are normally used. Recent international guidelines raised some concern about ESAs employment with a possible impact in CIA management and changes in clinical practice behavior.

Patients and methods. To evaluate opinions about CIA clinical management preference, AIOM Lombardia coordinators sent via e-mail to AIOM Lombardia onco-ematologist members a 12-item questionnaire about their knowledge on CIA and usual therapeutic strategies to manage this adverse event.

Results. From 01/2011 to 03/2011, 81 questionnaires were collected with an estimated share of 30%. The survey was completed mainly by oncologists (91%) with a median age between 35-50 years (50%). CIA was considered of clinical impact to change cancer therapeutic strategy in nearly 60% of the answers. ESAs were administered largely (80%) with concomitant iron supplementation in 52%; 38% jointly used blood transfusion as part of the therapy. Nearly 20% of respondents correctly employed transferrin saturation (TSAT) levels as a marker to guide iron supplementation. Physician prescribers strictly followed the guidelines to start and stop ESAs even if 14% were negatively influenced by new ASCO's recommendations. ESA biosimilars were considered future substitutes of originators in 45% of the cases.

Conclusions. CIA was perceived as adverse event with a mild impact on clinical practice. ESAs were largely employed, however the number of transfusions and lack of employment of markers of iron depletion suggested that adherence to guidelines could be theoretically met but with some discordances regarding the most appropriate strategies in daily clinical practice.

F26 "*DONATORI DI MUSICA*": A NEW APPROACH IN THE SUPPORTIVE CARE FOR PATIENT WITH CANCER

Toccafondi A.[1], Mambrini A.[1], Cantore S.[1], Bonacchi A.[2,3], Miccinesi G.[3], Prosseda R.[4], Ferrarini G.[1], Serenella E.[1], Orlandi M.[1], Cantore M.[1]

[1]Oncological Department, Carrara; [2]Centro Studi e Ricerca Roberto Assagioli, Istituto di Psicosintesi, Firenze; [3]Istituto per lo Studio e la Prevenzione Oncologica (ISPO), Firenze; [4]Art Director

Background. There is a growing interest in psychological and physiological effects of music alongside its use for therapeutic purposes. Since 2009, the Oncology Unit of Carrara's Hospital has been promoting a new experience called "*Donatori di Musica*" which aims to organise weekly live concerts in the oncology departments. Although this initiative has been spreading throughout several oncology units in Italy, the effects of the concerts on in-patients have never been investigated.

Aims. Firstly, to establish an accurate description of in-patients' attendance at the concerts and to correlate it with sociodemographic and clinical variables. Secondly, to investigate whether attending the concerts could influence in-patients' psychological conditions during their hospitalization. Thirdly, to identify concerts' aspects that could be related to better psychological effects.

Methods. An *ad hoc* form will be used to collect patients' socio-demographic and clinical information. At the moment of admission to the hospital and at discharge, 300 in-patients will fill in questionnaires to assess distress (DT), anxiety and depression (HADS). The STAY-Y test will be used to assess anxiety level of 150 in-patients before and after the concerts.

Results. Since January 2011, fifteen concerts have been performed in the ward. Preliminary results on 47 in-patients who attended the concerts show a reduction during the hospitalization in the score of distress from 4.5 to 3.5 ($p < 0.001$) and anxiety from 7.9 to 6.6 ($p < 0.001$). Conversely, no significant differences were found both among 47 in-patients hospitalized when there were no concerts and 12 in-patients who did not attend the concerts out of their choice. STAY-Y was filled in by 41 in-patients two hours before and two hours after the concert. The level of state anxiety decreased from 45 to 42.4 points ($p < 0.05$) while as expected trait anxiety remained stable (from 42.4 to 41.9).

Conclusions. Data suggests that attendance to *Donatori di Musica*'s concerts reduces in-patients state anxiety and most importantly improves their psychological conditions during hospitalization.

F27 AN INSIGHT INTO THE USE OF CHEMOTHERAPY (CT) NEAR THE END OF LIFE. A RETROSPECTIVE ANALYSIS

Trogu A., Mozzicafreddo A., Cristofano A., Malossi A., Alvaro M.R., Stella A., Sirotovà Z., Grasso F., Spinazzé S., Cucchi M., Numico G.

S.C. Oncologia, Azienda USL della Valle d'Aosta, Aosta

Background. The administration of CT near the end of life is a controversial issue. Good quality of palliative cares is considered the best way of achieving symptom control without the use of aggressive treatments. However, in daily clinical practice, many reasons, like pts expectations, difficulties in prognostication, young age, treatable tumour, high social level, high symptom burden, can induce to consider the use of CT.

In a large North-American series studied in 1996, the rate of CT use in the last 2 weeks of life was reported to be 18.5% (Craig C, JCO 2004). This figure could be considered a reference for the analysis of single-center data. Our study aimed at evaluating the use of CT in cancer patients who died in a 1-year period in our Region.

Methods. The study was conducted examining all the cancer pts who died in Valle d'Aosta region in 2009. Each patient file was examined and data about baseline features, disease and treatment features were collected.

Results. 197 pts dead in the examined period; median age was 68. 141 (71.5%) received CT; 35 (24.8%) in the last 4 weeks and 17 (12.0%) in the last 2 weeks of life. Of the pts treated with CT in the last 2 weeks, 10 (58.8%) were younger than 65; 13 (76.5%) had a solid cancer and 4 (23.5%) had hematological disease. Eight (47.0%) were at their first-line CT, while 9 (52.9%) were pretreated; in 13 (76.5%) cases CT was single agent, in 4 (23.5%) a polyCT. Death occurred in 12 (70.6%) cases for progressive cancer, and in 5 (29.4%) for an unexpected event.

Discussion. Compared with available data, our results suggest a low rate of CT administration in the last days of life. However, at least in some pts, the choice was not motivated only by clinical grounds. This suggests that subjective factors may influence the oncologist when facing with the cancer patient seeking further hope.

F28 GERIATRIC ASSESSMENT IN ONCOLOGY: A PROJECT OF COLLABORATION BETWEEN ONCOLOGIST AND GERIATRICIAN

Coialbu T.*, Pizzorni C.M.°

**Day Hospital Oncologico ASL 3 Genova, Ospedale A. Gallino; °Servizio di Geriatria ASL 3 Genova, Ospedale Celesia*

Introduction. Aging is an important risk of cancer. More than half of new cancers are diagnosed in elderly patients. Functional and cognitive impairments can increase the risk for adverse outcomes during diagnostic procedures and cancer treatments. Moreover comorbidities often obstacolate an adequate therapy. So survival is commonly shorter in older cancer patients because of delayed diagnosis, advanced disease and toxicity of treatments. The risk of utilizing ineffective therapies is high.

A geriatric assessment is not routinely measured in oncological Day Hospital but evidence is increasing that selected elderly cancer patients benefit from geriatric evaluation. A geriatric assessment can predict morbidity in older patients and contribute valuable information for risk stratification. However barriers to the assessment often include time, resources, healthcare providers. We decided a collaboration between Oncologist and Geriatrician by a preliminary measure of ADL (activities daily living) and IADL (instrumental activities of daily living).

Patients and methods. During the first 3 months in 2011 we evaluated 45 older >75 years patients visited and treated at Oncological Day Hospital. We administered them two questionnaires (ADL and IADL) to screen patients at risk of frailty or vulnerability. Median age was 80 (75-95). The majority of diseases were: breast cancer in 12 cases, gastroenteric in 10, haematological diseases in 9, lung cancer in 4, gynecological in 4, genitourinary in 3, others in 3. Out of these patients 22 cases had advanced and 23 limited disease.

We distinguished them into three groups: fit patients who can be treated with full doses of chemotherapy (high scores for ADL and IADL), unfit patients or frail candidated for only palliative care (low scores for ADL and IADL) and intermediate group that needs tailored treatments after multidisciplinary evaluation (Balducci L., 2000).

Results. The whole group of patients completed the questionnaires with assistance; median time to complete it was about 6 minutes. Median scores was 5.5 (1-6) and 6 (2-6) for ADL, respectively for advanced and limited disease, 5 (0-8) and 8 (0-8) for IADL, respectively for advanced and limited disease. We observed the following critical issues: limited resources, time and compliance of patients and/or caregivers during the interviews. However we could select 14 patients to be evaluated more carefully because of risk of vulnerability and/or poor compliance to therapy.

Conclusions. This brief geriatric assessment tool helps us to choose patients included in the "gray zone" (high score for ADL but low score for IADL). Next visit is planned at the ambulatory of the geriatrician to assess in addition to the functional status, cognitive function, psychological state, social support and nutritional status. An ulterior endpoint will be the caregiver training for managing oral chemotherapies and toxicities.

F29 DECREASED INCIDENCE OF OSTEONECROSIS OF THE JAW IN PATIENTS WITH BONE METASTASES TREATED WITH ZOLEDRONIC ACID

Di Trapani M.C., De Iuliis F., Russo I., Caporello P., Roselli A., Lauro S., Sarzi Amadè D., Pellegrini P., Marchetti P.

S. Andrea Hospital, La Sapienza University, Rome

Background. Bisphosphonates, as potent inhibitors of osteoclasts, are widely used in the management of metastatic bone disease. Bone metastases are associated with significant morbidity and mortality including fracture, hypercalcemia, spinal cord compression, and the need for surgery or radiation to bone. Any oral surgical procedure or traumatic event exposing bone to bacterial infection may precipitate osteonecrosis of the jaw (ONJ) in subjects who have been treated with bisphosphonates which suppress bone turnover and inhibit the angiogenesis associated with healing. Screening of the oral cavity and dental care was suggested as mandatory preventive measures of ONJ in patients receiving bisphosphonates.

Patients and methods. Our analysis includes patients affected by breast, lung and prostate cancer with bone metastases who received zoledronic acid since 2006. Patients with a previous use of bisphosphonates without a dental visit were excluded. 200 patients have undergone a baseline mouth assessment (dental visit + orthopantomography of the jaws) to detect potential dental conditions and dental care if required. Routine dental care, smoking habits, history of tooth extraction, use of dentures, and root canal therapy were recorded. The median dental follow-up (defined as the time between the first and last dental visits) was 6 months.

Results. None of our patients developed ONJ. Considering the patients exposed to zoledronic acid, the performance of a dental examination and the application of preventive measures led to a sustained reduction in ONJ.

Conclusion. The risk of developing ONJ after treatment of zoledronic acid is reduced (but not deleted) implementing the preventive measures, so ONJ is a manageable and preventable condition. Our results indicate that history of tooth extraction during zoledronic acid treatment increases the risk of developing ONJ. A multidisciplinary approach including oncohematologists and dental teams proved critical to better identify, prevent, and manage ONJ.

F30 OPEN COMMUNICATION BETWEEN CHILDREN AND THEIR PARENT WITH CANCER IS HELPFUL FOR COPYING WITH THE DISEASE AND MAINTAINING A NORMAL FAMILY LIFE

La Spina S., Lipari H., Parisi A., Catalano F., Pagano N., Giovinetto R., Urso O., Scollo P., Banna G.L.

Division of Medical Oncology and Breast Unit, Maternal-Infant Department, Cannizzaro Hospital, Catania, Italy

Background. The diagnosis of cancer involves the patient's family, and especially for the children is an event of high stress. Although it is difficult to find the right words to communicate to children, some studies have shown how this is important. In fact, children, even if they are very small, can perceive the changes, including the suffering of parents. The "not knowing" may generate negative and neglect fantasies in the child. This study aims to demonstrate how proper communication helps the child to cope with the suffering caused by the illness of her/his parent.

Methods. Twenty children, aged 4-18 years, belonging to parents diagnosed with cancer and receiving chemotherapy in 2011 year, were administered a first clinical interview with the following chart-projective tests: the test of the human figure and the test of the human family. The clinical interview ended with a recreational activity by the use of creative materials.

Results. A preliminary assessment of the clinical interviews and the above mentioned tests from the first 8 children, showed that 80% of children is scared and worried about the health of her/his parent. Seventy-five percent of children did not receive adequate communication from her/his parents, this being cause of suffering and stress. What most children felt is the lack of normal family life. Ninety percent of children said they hadn't explicitly expressed their fear and suffering because of their fear of hurting their parents.

Conclusions. Open communication within the family may lead to more effective ways of coping with the disease in those families where a parent has been diagnosed with cancer. Psychological support to those families may be helpful to foster the communication and normal family life.

F31 REHABILITATION AS A REINFORCEMENT OF THE SKILLS OF THE PERSON, THE SWAN PROJECT

Varese P.*, Bellingeri P.**, Musso M.***, Volgarino N.****

**Oncologo, **Nutrizionista-Palliativista, ***Psiconcologo, ****Infermiere Cure Domiciliari, ASL AL, Piemonte*

Background. The C.I.G.N.O. (swan) project was born in September 2006 giving reality to the need/desire to reorganize Oncology and Palliative Care Services in the former ASL 22 Piedmont, district of Ovada. The main target is to improve quality of life from diagnosis to the end of life for patients, families, professional caregivers and volunteers. The proposed model is alternative to the traditional one because workers, patients and families are first of all people and therefore they are "set" in a "level of energy" of mutual reinforcement and support.

Objective and methods. During residential weeks, patients, their families and few volunteers took part in a rehabilitation program in which food, relaxation sessions, art therapy, dance therapy, wellness therapy and focus on cancer issues were administered. A program in the program was a particular initiative, called creative journey-path, of art therapy (AT) and of dance movement therapy (MDT) that allowed individual participants to express themselves freely through predominantly non-verbal forms of communication (in paintings or body activities). Each participant at the beginning and at the end of the week rehabilitation has completed the following questionnaires: the distress thermometer, ESAS, CBA-VE.

Results and conclusion. The sample consisted of 30 subjects, evaluable questionnaires were 24, the average age was 64.33 (SD 12.72) 19 female, 5 male. To calculate the significance of the intervention was used The Wilcoxon Matched-Pairs Signed-Ranks Test.

Despite the diversity of backgrounds and complexity of cases recruited we found that:

- there were no dropouts in patients;
- no patient experienced worsening of symptoms present at the time of recruitment;
- no rescue doses of analgesics and other symptomatic drugs were asked or administered.

All patients reported a subjective improvement of wellbeing ($p < 0.0001$), ESAS pain ($p < 0.0008$), ESAS fatigue ($p < 0.0001$), ESAS depression ($p < 0.01$), ESAS anxiety ($p < 0.03$), thermometer of distress ($p < 0.0008$), CBAVE anxiety ($p < 0.0001$), CBAVE wellbeing ($p < 0.0001$), CBAVE perception of positive change ($p < 0.0001$), CBAVE depression ($p < 0.0001$) CBAVE perception of discomfort ($p < 0.001$).

F32 ROLE OF PAROXETINE IN THE TREATMENT OF ANTICIPATORY NAUSEA AND VOMITING IN CANCER PATIENTS: MULTICENTER EXPERIENCE

Pace R.[1], Sciacca V.[2], Capparella V.[1], Rossi R.[2], Rauco A.M.[1], Pistillucci G.[2], Lugini A.[1]

[1]Medical Oncology, Ospedale Generale "San Camillo de Lellis", Rieti, Italy; [2]Medical Oncology, Ospedale "Santa Maria Goretti", Latina, Italy

Background. Nausea and vomiting are acute side effects of chemotherapy most widely investigated. The nausea and vomiting that often accompany later treatments commence even prior to the chemotherapeutic agent being given, and this phenomenon has been defined as anticipatory nausea (AN) and vomiting. AN and vomiting is a learned response to one or more distinctive features of the chemotherapy clinic (conditioned stimuli) associated with the administration of emetogenic chemotherapy (unconditioned stimuli). Paroxetine is a potent selective serotonin reuptake inhibitor with indications for the treatment of depression. The purpose of this study is to test the efficacy and safety of paroxetine in the treatment of anticipatory nausea and vomiting in cancer patients undergoing chemotherapy.

Methods. From June 2009 to January 2011, 60 patients were included in the study. All patients were candidates for the execution of at least six cycles of chemotherapy and reported the occurrence of anticipatory nausea or vomiting after two cycles of chemotherapy. Response to treatment with paroxetine was assessed after each cycle of therapy from inclusion in the study. Was also evaluated the dose of paroxetine used more frequently and more effectively. Safety findings were also recorded.

Results. A total of 60 patients were included with a mean age of 70 ± 11 years. At inclusion all patients were enrolled to take

paroxetine drops 20 mg/day and in patients who did not benefit was increased the dose after each cycle, up to a maximum of paroxetine drops 60 mg/day. All patients were evaluated for effectiveness at each cycle of chemotherapy. 80% of patients reported disappearance of anticipatory nausea or vomiting at the first reassessment (paroxetine drops 20 mg/die); 10% of patients at the second reassessment (paroxetine drops 40 mg/die); 5% of patients at third reassessment (paroxetine drops 60 mg/die); 5% of patients non-responders. There was no significant toxicity experienced.

Conclusions. Paroxetine may be considered a drug of choice for the treatment of anticipatory nausea or vomiting in cancer patients.

F33 THERAPY AT CERTAIN TIMES AND RESCUE THERAPY, OUR EXPERIENCE IN PALLIATIVE CARE HOME

Tonetti R.[1], Massoni C.[1], Lavaselli P.[2], D'Amato D.[2], Murialdo R.[3]

[1]Oncologist, [2]Nurse, Palliative Care Service at home, District 12, ASL 3, Genoa; [3]Oncologist at the Department of Internal Medicine, "S. Martino" Hospital, Genoa

Introduction. In this study we present the observation data for a period of six months of cancer patients with advanced disease and rapidly evolving (Karnofsky performance status <50 with life expectancy <4 months) taken over by the care service palliative home of District 12 ASL 3 Genoa.

Objectives. The objective of this study was to evaluate the efficacy and tolerability of fentanyl buccal tablet (FBT), that is a new opioid formulation providing rapid-onset analgesia for the treatment of breakthrough pain (BTcP) in opioid-tolerant patients with chronic cancer pain.

Methods. In the period from February to July 2010 were taken into care in home care 61 cancer patients being treated for pain therapy. For proper evaluation of BTcP were formulated questions to patients according to validated systems. Twenty-eight patients were found to have BTcP: 16 women and 12 men, mean age 71 years. Primary tumour: breast 6, lung 5, gastrointestinal 4, pleura 3, bladder 3, ovary 2, pancreas 2, thyroid 1, parotid 1, uterus 1. Presence of bone metastases in 18 patients, intestinal obstruction in 3 patients. The assessment of pain corresponded to a mean baseline NRS of 3. All 28 patients were treated with opioids and adjuvant drugs. A patient with epidural catheter with continuous infusion of morphine and bupivacaine. Average daily number of episodes of BTcP 2.08. Average time of onset of BTcP: 3 minutes. Average intensity of episodes of BTcP measured by NRS: 7. Average duration of BTcP episodes: 23 minutes. Treatment of episodes of BTcP before the availability of the FBT: 19 patients were already treated with paracetamol, cortisone, oral morphine, oxycodone as paracetamol, morphine parenteral use. All 28 patients received treatment with FBT: 24 patients received daily FBT, 4 patients received FBT occasionally. For all patients, the dose of FBT was titrated: 18 patients needed a dose of between 100 and 200 mcg of FBT day; 2 patients maintained an average dose of 400 mcg, for week; 4 patients needed a dose of 600 mcg of FBT day; 4 patients needed a dose of 800 mcg of FBT day.

Results. Good response on pain assessed by NRS: T0 NRS 9 after FBT NRS 3. Response after just 10 minutes after FBT and maintained for more than 60 minutes. Only 2 of 28 patients reported side effects (dizziness, vomiting) and chose to discontinue therapy. The drug had a very good overall acceptability, there wasn't any trouble during opening the package which has a security system and during the taking of the tablet.

Conclusions. The advantages of fentanyl buccal tablet, both in terms of pharmacokinetics and compliance, make it a drug of choice in the treatment of BTcP, allowing a more rational and targeted symptom management, giving a good and prompt therapeutic response and control of side effects of opioids due to the short duration of action.

F34 ASSESSMENT OF SAFETY AND EFFICACY OF ORAL LIPOSOMAL IRON SUPPLEMENTED IN CANCER PATIENTS WITH CHEMOTHERAPY-RELATED ANEMIA RECEIVING EPOETIN ALFA

Mare M., Mafodda A., Prestifilippo A., Blanco G., Sciacca D., Vitale M.P., Giuffrida D.

Istituto Oncologico del Mediterraneo, Viagrande, Catania

Background. The concomitant use of oral iron as a supplement to erythropoiesis-stimulating agents in patients with chemotherapy-induced anemia is controversial. Liposomal iron (LI) is the new oral formulation that avoids patient gastrointestinal discomforts which are usual during iron supplementation. Thanks to the liposome technology, bioavailability of iron increases by 3.5 times compared to the same iron source with non-liposome form. This study was designed to evaluate the safety and efficacy of supplemented administration of oral LI to increase hemoglobin (Hb) in anemic cancer patients receiving chemotherapy and epoetin alfa.

Methods. A total of 57 patients, age 39-76 years, with chemotherapy-related anemia (Hb <10 g/dL; serum ferritin ≥100 ng/mL or transferrin saturation ≥15%) to receive chemotherapy and epoetin alfa (40,000 U weekly) to 8 weeks plus oral LI. Posology of LI was 30 mg once daily for 8 weeks. Primary endpoint of the study was an increase in Hb level from baseline, red blood cell transfusion and the safety profile of LI. Quality of life (QoL) with FACT-An questionnaire was also evaluated.

Results. Fifty-seven patients were evaluable for efficacy and safety. The percentage of patients with hematopoietic responses was high (only 4 patients showed no response to therapy). From baseline to study end, a mean increase in HB levels of 2.3 g/dL was noted. None of the patients required red blood cell transfusion and supplemented administration of oral LI was well tolerated in all patients. Improvement in QoL parameters was observed in all patients.

Conclusions. Our results suggest that for cancer patients with chemotherapy-related anemia receiving supplemented epoetin alfa, daily supplementation of LI is safe and produces a significantly increase in Hb anemia with improved QoL. The increase of HB is similar to the ones observed with the use of IV iron supplementation in several studies. Taking into consideration physician's convenience and patient's compliance, this regimen offers an optimal alternative to IV iron supplementation.

F35 BURDEN OF HYPERTENSION WITH BEVACIZUMAB: FREQUENCY, PATHOGENESIS, COMPLICATIONS, MANAGEMENT AND PREDICTIVE ROLE

Petrelli F.[1], Dognini G.[2], Cabiddu M.[1], Borgonovo K.[1], Locatelli G.[2], Cagnoni F.[2], Destro M.[2], Barni S.[1]

[1]Medical Oncology Department, [2]Internal Medicine Department, Azienda Ospedaliera Treviglio-Caravaggio, Treviglio (BG)

Background. Hypertension (HTN) is one of the most frequent co-morbid conditions found in cancer registry patients and observed side-effect of systemic inhibition of vascular endothelial growth factor signaling, in particular with bevacizumab (B). Incidence, pathogenesis, treatment and predictive role of HTN in B-treated patients (pts) are reviewed in this paper.

Methods. A PUBMED search was performed ("hypertension and bevacizumab"), and 334 papers were retrieved and reviewed.

Results. In a meta-analysis of 12,656 cancer pts from 20 studies the incidence of all-grade HTN in patients receiving B was 23.6%, with 7.9% being high-grade (3 or 4). The mechanisms leading to B-induced HTN are thought to involve: decreased nitric oxide (NO) production, increased vascular resistance and rarefaction and neurohormonal factors. Moreover, B-induced HTN is dose-dependent. Recently B was found to be associated with fatal events (RR 1.46), in particular cerebrovascular accidents (incidence 0.7%; RR 3.6). No clear recommendation for any antihypertensive agent can be made because of the lack of controlled studies addressing the subject. In the BriTe study angiotensin-converting enzyme inhibitors (ACE-Is) (33.3%) and β-blockers (29%) were most commonly used to manage *de novo* HTN. Among calcium-channel blockers (CCB), amlodipine and felodipine are the preferred ones, while non-dihydropyridine CCB (e.g diltiazem and verapamil) should be contraindicated or used cautiously (because of CYP3A4 metabolism). In 2 recent meta-analyses, a possible role of angiotensin-receptor blockade in cancer development was hypothesized. Conversely ACE-Is demonstrated cytostatic effects. Some other studies reported a better cancer prognosis in patients developing HTN.

Conclusions. HTN is a frequent adverse event with B treatment in solid tumours. Despite these pts are usually treated like general hypertensive population, the use of ACE-Is and β-blockers (both inducing NO release) might be preferred. Moreover, the prognostic implications of HTN development, the possible cytostatic effect of ACE-Is, and the management of HTN itself deserve to be better defined, possibly in clinical trials, in order to find an optimal and tailored approach to these patients.

F36 USEFULNESS OF A REHABILITATION PROGRAM FOR COLORECTAL CANCER (CRC) PATIENTS WITH OXALIPLATIN-INDUCED POLINEUROPATHY

Tolli V.S.[1], Mattei F.[2], Leone G.[1], Mereu M.L.[1], Bonassi S.[3], Grenga I.[4], Cesario A.[3], Formica V.[4], Roselli M.[4]

[1]San Raffaele Institute Velletri, Rome, Italy; [2]Unit of Clinical and Molecular Epidemiology, [3]Scientific Direction, IRCCS San Raffaele Pisana, Rome, Italy; [4]Tor Vergata Clinical Center University of Rome, Medical Oncology Unit and IRCCS San Raffaele, Rome, Italy

Background. Patients treated with oxaliplatin often develop neuromotor polyneuropathies that can lead to disability in both motor and independence areas, with negative consequences on quality of life (QoL). Aim of this study was the methodological validation of a dedicated neuro-rehabilitative program (NRP) in radically resected (rr) CRC patients who developed iatrogenic polyneuropathies after oxaliplatin-based adjuvant chemotherapy.

Methods. rrCRC patients treated with standard 6-month adjuvant chemotherapy (FOLFOX-4 regimen) at Tor Vergata Clinical Center (Rome) between December 2009 and March 2010, who developed persistent oxaliplatin-related neuropathy, after 1 year of uneventful follow-up, were addressed to the Neurorehabilitation Unit of San Raffaele Institute, Velletri (Rome) to be evaluated for inclusion in a NRP focused on functional recovery. The NRP covered a three-month period with three day-care accesses a week, each access lasting 4 hours. The program included: 1) motor proprioceptive exercises + gait re-education + exercises for balance and coordination (360 min/week); 2) occupational therapy for training in activities of daily living (270 min/week); 3) psychological treatment (90 min/week). Outcome measures were: electroneurography examinations (ENG), polyneuropathy dysfunction scores (Dyck Scale), and the Modified Barthel Index (BI), all assessed before the NRP and then at regular monthly intervals up to three months post-NRP conclusion.

Results. As of April 2011, fourteen patients were enrolled, 7 of them were diagnosed with a non disabling polyneuropathy and therefore did not start the NRP and are currently followed up three-monthly. Only three patients completed the NRP (all females, mean age = 63.3±3.5), for all of them ENG findings showed unchanged motor-sensitive polineuropathy, while neurological symptoms were reduced in all subjects and the Dyck scale decreased by 50% to 5%. The three patients also shifted from a condition of mild disability to the complete independence, as assessed by BI.

Conclusions. Not surprisingly ENG data, documenting the presence of polyneuropathy, did not change. That is because the NRP acts on the motor performances, using alternative approaches to compensation. However, patients improved in terms of independence and clinical performances demonstrating that NRP is feasible and may positively impact on QoL

F37 MAKE-UP SESSIONS DURING CHEMOTHERAPY HELP WOMEN TO GET CONFIDENCE WITH DIAGNOSIS AND TREATMENT OF THEIR CANCER

La Spina S., Lipari H., Parisi A., Catalano F., Pagano N., Giovinetto R., Urso O., Scollo P., Banna G.L.

Division of Medical Oncology and Breast Unit, Maternal-Infant Department, Cannizzaro Hospital, Catania, Italy

Background. Cancer treatment has the potential to be devastating to the self-esteem since adverse effects may result in major changes to patients' appearance, like hair loss and skin problems. The impact of cancer treatment may result in poorer psychosocial adjustment and reduce quality of life. The women's body during cancer becomes a metaphor for a devastating experience. Next to the anger, confusion and anxiety that follows the diagnosis, feelings of humiliation, shame, embarrassment may appear, as a reaction to negative body image perceptions. The make-up sessions provide the opportunity to share feelings with others who are experiencing similar physical changes, and becomes an important part of the psychological support process. Taking care of patients appearance may help patients to feel attractive and comfortable with their bodies again.

Methods. This prospective study will follow 100 women, aged 30-70 years, undergoing chemotherapy in 2011 year, with a

diagnosis of breast, ovarian or lung cancer. The make-up sessions are organized once a month during chemotherapy treatment. The adherence is evaluated on the basis of a psychological interview, and an anonymous questionnaire to be completed at the end of each make-up session.

Results. From the questionnaires completed at the end of the first make-up session (n = 12 patients), the following results were reported: 80% of women felt more relaxed; in 60% the desire to go out has increased; 80% felt more feminine; 85% stated that meeting with other women sharing the same experience help them feeling less alone during the cancer treatment; 90% reported the make-up session help them spend hours of treatment more quickly and with less adverse effects as well as intrusive thoughts.

Conclusions. The make-up sessions during chemotherapy offer support for women affected by cancer, allowing them to feel better about themselves, so they can approach cancer treatment with greater confidence. Furthermore, the opportunity of sharing the experience of cancer treatment may result in psychological benefits and reduce distress provoked by body image changes.

F38 PATIENTS' SATISFACTION ABOUT PREVENTIVE AND CURATIVE UTILIZATION OF VITAMIN K1 BASED CREAM IN SKIN TOXICITY FROM CETUXIMAB FOR METASTATIC COLORECTAL CANCER

Pinta F., Ponzetti A., Spadi R., Fora G., Fanchini L., Zanini M., Ciuffreda L., Racca P.

ColoRectal Cancer Unit, Medical Oncology 1, Hematology and Oncology Department, A.O.U. San Giovanni Battista, Turin

Background and methods. Cetuximab is a component of systemic treatment for K-Ras wildtype metastatic colorectal cancer (mCRC). Nearly all patients develop a skin toxicity, mainly acneiform rash. Interest about this dose-limiting side effect is increasing. Vitamin K1-based (phytomenadione 0.1%) cream has demonstrated benefits in early trials for prevention and treatment of cetuximab-induced acneiform rash. We distributed vitamin K1 cream to patients undergoing chemotherapy plus cetuximab for mCRC and collected data about skin toxicity and patients' compliance and satisfaction using a specific questionnaire.

Results. From November 2010 to April 2011, vitamin K1 cream was administered to 24 patients treated with cetuximab for mCRC. Sixteen were male with a median age of 69 years. Twelve patients had a single metastatic site; 15 had metastasis to liver and 11 to lung. Two patients were receiving a first-line therapy and 22 were pretreated. No patient had significant cutaneous comorbidity. Twenty-three patients applied vitamin K1 cream twice a day mainly on face and trunk; only one patient did not apply it because of treatment interruption at first cycle due to G3 diarrhoea. Thirteen patients used the cream before the development of skin rash while eleven started it when rash was already present. Twenty-three patients developed acneiform rash; the maximum grade of skin toxicity according to CTCAE v.3.0 was G1, G2, G3 or G4 in respectively 8, 9, 4 and 1 patient; for 18, 3 and 1 patient it was rash, xerosis and paronychia. Only 5 patients needed a dermatologic consultation. Twelve patients defined themselves very satisfied with the treatment, equally distributed among the prophylaxis and treatment group. Six patients reported an additional benefit on itch and xerosis. No adverse events were reported using vitamin K1 cream. Seven patients did not report any benefit.

Conclusions. Discordant patients' reporting need to be confirmed in further evaluations of vitamin K1 cream for prophlyaxis and treatment of cetuximab induced skin rash in mCRC.

F39 COMPASSIONATE CARE: NOT JUST A PATIENT

Ravaioli V., Berardi M.A., Meggiolaro E., Conficconi A., Tedaldi R., Bragagni M., Tison C., Bertelli T., Amadori D.

Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), Meldola (FC), Italy

Background. Cancer has a significant impact on quality of life; it can be life changing, not only for associated health problems, but also for psychological and relational distress. It frequently leads to isolation and silence, and triggers a considerable change in the lifestyle and the personality of sufferers. Two projects have been created involving all IRST's patients: *Harmony Corner* and the *Expressive Writing Workshop*. The primary objectives are to improve quality of life and to give patients the opportunity to express themselves and their needs. The secondary objectives are to provide personal care services, to improve body image and self-perception, and to rework and share personal experiences in a group setting.

Methods. *Harmony Corner* offers a full range of personal grooming services to sufferers. Two questionnaires are distributed at service entry and exit, the former to collect clinical, self-perception, and motivation data, and the latter to assess the level of satisfaction. The *Expressive Writing Workshop* helps 10 persons to experience a new way of expressing themselves, supported by an oncology psychologist. Two questionnaires are distributed: one at the end of each session to get valuable feedback from the workshop just lived, the other is presented during an interview at the end of workshop to analyze the short- and medium-term benefits.

Results. The projects were started in October 2010 and are still ongoing. Preliminary results show that there is complete acceptance and satisfaction for both initiatives. *Harmony Corner* combats the effects of therapy, improves self-image, and allows sufferers to be and to feel pampered. The *Expressive Writing Workshop* provides a forum for sufferers, giving voice to their emotions, breaking the silence associated with this disease.

Conclusions. These services are designed to add value to the quality of therapy. All those surveyed agree that this kind of attention to personal wellbeing is the difference between a conventional Hospital and an Institute of excellence.

F40 MONOCENTRIC RETROSPECTIVE STUDY ON THE USEFULNESS OF SYSTEMIC ANTIBIOTIC PROPHYLAXIS AFTER GUIDEWIRE REPLACEMENT OF INTERMEDIATE-TERM VENOUS CENTRAL CATHETER IN ONCOLOGIC PATIENTS

Gasparro D., Tarasconi S.*, Fontana E., Bella M., Ardizzoni A.

*Medical Oncology Unit, *Emergency Department, University Hospital of Parma*

The insertion of Hohn central venous catheters and the management of catheter related complications are performed in our

oncologic center by a unique health care physician, and this has allowed an accurate analysis of the catheter dysfunctions occurred over the years (absence of blood reflux, partial or complete obstructions, cutaneous infection at suture site, etc.), solved by the dispositive replacement.

When a catheter dysfunction occurs, we usually opt for a guidewire exchange, that allows to avoid the risk of pneumothorax and to reduce the patient X-ray exposition.

After the catheter replacement, the clinician who sent the patient for the dispositive exchange is free to determine whether to administer a systemic antibiotic prophylaxis or not.

Since 1997, on the basis of results of a meta-analysis of 12 randomized trials of catheter replacement, we know that CVC guidewire exchange may be associated with a greater risk of bloodstream infections than new-site replacement.

The purpose of our study was to determine whether post-replacement systemic antibiotic prophylaxis could reduce the risk of infective complications.

We considered for our retrospective study all the oncologic patients who had undergone a guidewire central venous catheter replacement in our center between February 2009 and April 2011. Among them, 80 patients were eligible for our study, 40 of which had been treated with antimicrobial prophylaxis.

From the analysis of the collected data we found that none of the 80 patients had infectious or thrombotic complications within 60 days after catheter replacement.

The results of our study indicate that the guidewire replacement of CVC, performed by experienced physician, is a safe methodology and, in contrast to the data of meta-analysis, isn't associated with an increased risk of systemic infections.

In summary, on the basis of our data, although collected on a small series of patients, we can conclude that the administration of systemic antimicrobial prophylaxis after a guidewire CVC replacement in order to prevent catheter-related infections is unnecessary and potentially detrimental.

F41 MOOD DISORDERS IN THE CANCER POPULATION

Locatelli C., Cicerchia M., Repetto L.

UOC Oncologia, INRCA-IRCCS, Roma

Objective. Cancer is an important trigger for new onset of psychiatric symptoms in the cancer population, especially in the aging population. Despite progress in our knowledge in the psycho-oncology area, there is a scarcity of studies on the psychological impact of cancer and the prevalence of mood disorders in the elderly. Mood disorders impact on quality of life, anticancer treatment compliance, hospital stay duration, health-care costs, morbidity and possibly mortality. We performed a cross section study with the aim to examine the distribution of mood disorders in the adult and in the senior adult cancer population.

Materials and methods. All eligible patients were administered a battery of tests for psychiatric and cognitive assessment. To shed light on the incidence of mood disorders in the cancer population, especially in the elderly population, the following variables, patient's age and cognitive status, cancer types and stage and oncologic treatments were assessed. The neuropsychological battery includes: (MMSE); Rey auditory verbal learning; Rey complex figure; Progressive Raven's Matrixes, Stroop, WCST, FVF.

The psychopathological battery includes: SCIDII; HDRS; HAMA; SQ; TAS-20; ISS; SSI; QL-INDEX; CIRS. STAI-Y 1/STAY-Y2; FS. Patient recruitment is ongoing.

Results. 197 pts were recruited in 5 Centers: 39 are males, 148 females. Mean age is 54 (range 21-83). The distribution for tumour types was: 49 ovarian cancer, 34 colon-rectum, 50 breast, 19 lung, 20 uterine, 24 other tumour types were observed. Ninety-nine patients present advanced disease (stage III-IV). 157 patients were receiving chemotherapy: 77 adjuvant chemotherapy, 89 treatments for advanced disease, 31 biologic therapies. Depressive disorders were observed in 61 pts (31%) and generalized anxiety disorders in 59 (30%). Thirteen (6%) pts were treated for depression and 42 (21%) for anxiety at the time of interview.

Conclusions. Mood disorders are frequent in cancer patients but are still underestimated and under-treated. Information programs and specific training are necessary to improve the awareness of clinical oncologists and to provide them with tools for the assessment and management of mood disorders in cancer patients.

F42 MEASURING PAIN IN PATIENTS UNDERGOING CHEMOTHERAPY IN AN ONCOLOGICAL DAY HOSPITAL

Cabiddu M., Borgonovo K., Petrelli F., Cremonesi M., Olejnik K., Barni S.

Medical Oncology Division, A.O. Treviglio-Caravaggio, Treviglio, Italy

Introduction. Independently of the stage of disease, 53% cancer patients experience pain.

The pain Visual Analogic Scale (VAS) is an useful, cost-effective and rapid means of measuring pain in every kind of patient, independently of his level of schooling and compliance. This study was to measure the percentage of pain in our Day Hospital (DH) patients. The results obtained by an oncologist and a nurse were then compared and any discrepancies examined.

Material and method. From January 2010 to February 2011, 154 patients were evaluated with an average number of admissions per patient of 10/patient (total admissions: 1546). Median age was 64 years, 70 males (45.5%) and 84 females (54.5%); 89 patients (57.8%) had advanced or metastatic disease and 65 (42.2%) were undergoing adjuvant therapy. All patients were affected by solid cancers: GI cancer 44.2% (43 males, 25 females), lung cancer 14.9% (17 males, 6 females), breast cancer 33.1% and 7.8% (12 patients) other cancers. 42/154 patients (27.3%) had attended high school and 8/154 (5.2%) had a degree.

Results. 70.8% patients (109/154) reported pain in 31.4% (485) of the 1546 daily DH admissions. Of the 109 patients reporting pain, 39.4% were undergoing adjuvant therapy, and 61.6% palliative or curative treatment.

The majority of patients had attended only primary school (71.6%).

The VAS scores of 8/109 patients (7.3%) and 80/485 admissions (16.5%) could not be evaluated.

At least one discrepancy was observed; there were at least 2 points of difference in the VAS scores recorded by the oncologist and the nurses in 70/109 patients (64.2%) and in 175/405 admissions (43.2%).

Conclusion. The incidence of pain noted in patients undergoing chemotherapy in our DH is higher than that mentioned in literature. One must take into consideration that these patients have active disease or recently undergone surgery. The high percentage of discrepancy in the measurement of pain provides an opportunity for further studies to understand these results.

F43 MEASURING PAIN IN ONCOLOGICAL DAY HOSPITAL (DH) PATIENTS - DISCREPANCIES

Borgonovo K., Cremonesi M., Cabiddu M., Petrelli F., Olejnik K., Barni S.

Medical Oncology Division, A.O. Treviglio-Caravaggio, Treviglio, Italy

Introduction. Patients are often reluctant to communicate the pain they feel.

The percentage of pain in patients was measured in our Day Hospital by an oncologist and a nurse and the values recorded were compared. We wanted to study any discrepancies and hence suggest the possible reasons for them.

Materials and methods. From January 2010 to February 2011, we evaluated 154 patients (total DH admissions: 1546). 70.8% patients communicated pain in 485 admissions. Pain was measured by both an oncologist and a nurse using the pain Visual Analogic Scale (VAS) and by a nurse alone using the Happy Face Pain Rating Scale (PRS).The discrepancies were defined by at least 2 points of difference on the VAS score between those measured by the oncologist and the nurse, or between the scores obtained by the nurse using the VAS and PRS scores.

Results. The following discrepancies were observed: in 18/101 patients (17.8%) and 38/405 admissions (9.4%) the VAS score recorded by the oncologist was greater than that registered by the nurse; in 52/101 patients (51.5%) and 137/405 admissions (33.8%) the opposite was noted. In 71.3% of patients and 76.8% of DH admissions the discrepancy was noted between the VAS score and PRS score recorded by the nurse; in 257/311 admissions the PRS score was greater than the VAS score whereas in 54/311 admissions the opposite was observed. In 32/101 patients (31.7%) and 58/405 admissions (14.3%) the discrepancy was greater than 2 points.

Conclusion. Our results appeared to confirm the reluctance of patients to reveal their pain, especially to the oncologist.

Even the registration performed by the nurses using two different methods did not give the same results. One of the reasons could be due to the difficulty which patients with a lower level of education have (67.5% patients) when being asked to give a numerical value to the intensity of their pain. The best instrument for measuring pain has yet to be found.

F44 INTRAPERITONEAL BEVACIZUMAB IN MALIGNANT ASCITES

Cengarle R., Pisanelli M.B., Rossi A., Adami F., Cavazzini M.G., Aitini E.

Struttura Complessa di Oncologia ed Ematologia, Azienda Ospedaliera Carlo Poma, Mantova

Malignant ascites is a common complication of advanced cancers. Various studies have shown that malignant effusions arise in part from increased production and activity of vascular endothelial growth factors VEGFs. Some experiences demonstrate safety and efficacy of intraperitoneal administration of bevacizumab at 5 mg/kg in ovarian and other malignant ascites. Between March 13th, 2010 and January 18th, 2011 we treated with intraperitonel bevacizumab (5 mg/kg) four patients with refractory malignant ascites from ovarian (2 patients) and breast (2 patients) cancer. The performance status was 0 in one patient, 1 in two patients and 4 in one patient. The age was from 49 to 74 years. All patients had cytologically documented malignant ascites, refractory to systemic chemotherapy, and two patients refractory to intraperitoneal chemotherapy with cisplatin plus AraC. All patients need repeated paracentesis (weekly or twice a week). All patients tolerated well the treatment without complications. Three patients experienced prolongation of interval between paracentesis following IP bevacizumab (from 7 weeks to10 weeks). Two patients repeated the treatment with benefit when ascites developed again (one patients twice, once four times). One patient died 21 days after for cachexia.

Conclusions. In our experience intraperitoneal bevacizumab is a relatively safe and highly efficacious way to palliate the symptoms of refractory malignant ascites.

F45 STREAM: A SUCCESSFUL PROJECT TO MANAGE SKIN TOXICITY IN PATIENTS WITH HEPATOCELLULAR CARCINOMA AND METASTATIC RENAL CELL CARCINOMA TREATED WITH SORAFENIB. EXPERIENCE FROM A DAY HOSPITAL

Scandurra G., Aiello R.A., Alì M., Taibi E., Dimarco R., Mazzola A., Chiarenza M., Sanò M.V., Fallica G., Miano E., Caruso M.

UF Oncologia Medica, Humanitas Centro Catanese di Oncologia, Catania, Italy

Introduction. Sorafenib is an oral small molecule multi-target for the treatment of patients with hepatocellular carcinoma and advanced renal cancer. The most frequent side effect of sorafenib are: rash (34%), hand foot skin reaction (27%), diarrhoea (33%), hypertension (11%). The novelty of the drug requires a multidisciplinary team. In particular, the nurse who provides the administration of skin care kits - thanks to the privileged position of closeness and intimacy - can be responsible for the education of the patient, making better compliance to treatment.

Proposal. Evaluating the effectiveness of specific dermatological kit, identifying the perception of the severity of the problem of skin toxicity by the patient, the compliance and determine whether the integrated management of this toxicity is useful to reduce interruptions of therapy due to skin toxicity.

Materials and methods. Since 11 May 2010 to 28 February 2011, sorafenib was administered to 15 patients (3F/12M; median age 72 years, range 46-79), 7 affected by kidney cancer and 8 by hepatocellular carcinoma.

The nurse provided dermatologic skin care kit and used to evaluate cutaneous toxicity by collecting images, tests and writing journal during the baseline and during the treatment.

Results. Just 2 patients out of 15 interrupted the treatment due to AE HFSR G2. Visits more frequent (every 10-15 days) have an impact on reducing the symptoms of hand-foot skin reaction syndrome. This kind of treatment has a double effect: giving pain and emotional relief because the patient perceives care. Test results have shown how much important is the presence of the nurse in any disabling HFSR.

Conclusions. The integrated medical care with nurse assistance has succeeded in fighting cutaneous toxicities caused by sorafenib, with effective outcomes in reducing treatment inter-

ruption and providing objective and psychological relief to the patient.

F46 CANCER-RELATED ELECTROLYTE CHANGES: PARANEOPLASTIC SYNDROMES AND IONIC DISORDERS CHEMOTHERAPY-BASED. REVIEW OF LITERATURE AND BRIEF INDICATIONS OF MANAGEMENT

Nastasi G., Galdy S., Cotroneo G., Mauri C., Pezzoli N., Duluc M., Ravenda S., Rodà G.

U.O. Medical Oncology, A.O. Bolognini, Seriate (BG)

Background. Changes in fluid and electrolyte balance are common in oncology. There are two main groups of this complication: forms directly related to the malignant disease, the so-called paraneoplastic syndromes, and forms related to toxicity by chemotherapy.

However, while the first ones are sufficiently known, the second ones are often not recognized. In addition, iatrogenic fluid and electrolyte abnormalities are not caused solely by the classic chemotherapies, but also by the target therapies (monoclonal antibodies and small molecules).

Aim. Study of the major electrolyte abnormalities in oncology and brief advices of therapy.

Methods. Review of the literature.

Conclusions. The most common paraneoplastic syndromes are: malignant hypercalcemia, hyponatremia from inappropriate secretion of ADH, hypokalemia from ectopic ACTH secretion. On the other hand, hypocalcemia, hypernatriemia, hypokalemia, hyper- and hypophosphatemia, are some of electrolyte abnormalities secondary to the use of anticancer drugs. The mechanisms underlying these disorders are different: emetic and gastrointestinal toxicity, nephrotoxicity, drug-specific damage. Therefore, the aim of this study is to focus on the major metabolic disorders in oncology, also on the less known and therefore more insidious, and to give some short therapeutic advices.

F47 FAMILY MEMBERS' PERCEPTION OF PALLIATIVE SEDATION FOR TERMINALLY ILL PATIENTS ADMITTED TO HOSPICE

Paganini G.[1], Bonatti G.[1]. Roviello G.[2], Francini E.[2], Miano S.T.[2], Pascucci A.[2], Francini G.[2]

[1]Hospice of A.S.P. "Villa Carpaneda" Nursing and Rehabilitation Home, Rodigo (MN); [2]Medical Oncology, University of Siena

In September 2009 we interviewed, by means of anonymous questionnaire, 47 families (32 females and 15 males) of patients receiving palliative sedation at the end of life between August 2005 and August 2009 at the Hospice of A.S.P. "Villa Carpaneda" in Rodigo (Mantova). This study aims to analyze, retrospectively, how palliative sedation was perceived by family members. The data collected showed that the majority of respondents felt involved by the team of physicians and taking part in the choice of sedating, which did not give rise to any guilty feeling. However, still according to respondents, there was a low level of participation of the patient in the decision making process. Even if observing that the majority of caregivers thought about the period of sedation as an event necessary to alleviate the suffering, it is noteworthy that a significant percentage of them has lived it as an anticipation of the definitive separation from their beloved. However, only in two cases the practice of palliative sedation was perceived as an act of euthanasia.

F48 RITUXIMAB: MANAGEMENT OF HYPERSENSITIVITY REACTIONS

Mazzola A., Stabile C., Oliveri A., Pulvirenti S., Sciannaca A., Ciancitto R., Musumeci L., Longhitano M., Reale S., Bagnato S., Caruso M.

Humanitas Centro Catanese di Oncologia (CCO), Department of Medical Oncology, Catania, Italy

Many cancer therapies administered by IV infusion, including monoclonal antibodies, have the potential for infusion reactions. These require prompt, accurate assessment and management to avoid severe adverse events, including fatality. Monoclonal antibodies have an unique side effect profile due to the potential for non-allergic reactions caused by cytokine release. Rituximab is a chimeric anti-CD20 monoclonal antibody. Its intravenous administration is associated with substantial infusion-related toxicity. Recommended infusion durations are prolonged (average 5-6 h for first infusion and 3-4 h for subsequent infusions). Severe events occur occasionally and typically within 2 hours from the first infusion and are generally mild-to-moderate reactions that can be managed by either temporary interruption or administration of supportive care including corticosteroids, oxygen, or intravenous fluids. Premedication with antihistamines, paracetamol, and/or corticosteroids is a common practice to prevent reactions with all monoclonal antibodies.

Our aim was to explore the safety and tolerability of test dose infusions of rituximab in non-Hodgkin's lymphoma patients. Adult oncology patients diagnosed with non-Hodgkin's lymphoma and receiving rituximab were included in the study. From May 2005 to February 2011 ninety-eight patients were enrolled. The majority of them were treated with rituximab and CHOP or CHOP-like regimen. The schedule of administration for cycle one was 20% of the dose of rituximab unaltered and delivered according to the product monograph (5-6 h) in 500 mL sodium chloride; the remaining 80% dose on day two. All subsequent cycles were administered at full dose over a total infusion time of 3-4 h. Patients were observed for related reactions during the rituximab infusion and for 30 min after that. In addition, patients were asked to report any adverse reactions occurring within 24 hours. From May 2005 to February 2011, ninety-eight patients with non-Hodgkin's lymphoma were treated with the above schedules. The test infusion was well tolerated without any grade 3/4 adverse events observed. Our institution has thus adopted this as routine practice for all patients treated with rituximab.

F49 SURVEY ON DIAGNOSTIC AND THERAPEUTIC SKILLS ABOUT CANCER PAIN IN A REGIONAL HOSPITAL AND IN GENERAL PRACTITIONERS

Luzzani M.[1], Pasa A.[2], Molinari E.[1]

[1]S.S.D. Cure Palliative, Dipartimento di Gerontologia e Scienze Motorie, [2]S.C. Oncologia Medica, E.O. Ospedali Galliera, Genova

Background. Cancer pain in earlier stages is only a symptom (30%), while in advanced patients, because of high prevalence (60-90%), often becomes a real disease (Foley). Patients with chronic cancer pain and BTcP experience severe pain, greater functional impairment and more psychological distress, including depression and anxiety, than those patient without BTcP (Caraceni, Portenoy). BTcP in association with chronic cancer pain has also a greater socio-economic impact than cancer pain alone (Fortner). Unfortunately recent data suggest that neoplastic patients have high risk of undertreatment (Valeberg).

Aim. To be able to identify prevalence of chronic cancer pain and BTcP and different therapeutic strategies in two different settings: regional hospital and home care.

Material and methods. Observational survey, with a questionnaire (16 items), given to a sample of hospital physicians and general practitioners, about skills and different behaviours to recognize chronic cancer pain and BTcP and to prescribe therapeutic schedule.

Preliminary results. We delivered 89 questionnaires, whose 59 (60%) were completed: 36 (61%) by males, 23 (39%) by females, mean age 48.7. The definition of BTcP resulted unclear in 31%. In clinical experience physicians treat "often" (48%) and "every now and then" (46%) chronic cancer pain; they also treat "often" (27%) and "every now and then" (63%) BTcP. They reported that chronic cancer pain is not easy to treat and it is often necessary to redefine the analgesic therapy (84%); 42% of interviewed obtain adequate chronic pain relief in 70-90% of treated patients, while only 30% in BTcP. Physicians have evaluated in BtcP treatment morphine i.v. (30%) and ketorolac sublingual and i.v. (49%) as more rapid drugs. The same drugs are considered those with the best therapeutic index. Moreover the favourite routes of administration result: oral (38%), i.v. (18%) and sublingual (18%).

Conclusions. These results show the difficulty in treating cancer pain and in particular BTcP because often is unacknowledged and more adequate drugs aren't used.

F50 PEGFILGRASTIM INDUCED BONE PAIN PROPHYLAXIS WITH CODEINE/ACETAMINOPHEN AND ITS IMPACT ON QUALITY OF CARE IN BREAST CANCER ADJUVANT SETTING AT HUMANITAS CENTRO CATANESE DI ONCOLOGIA

Alì M., Aiello R.A., Scandurra G., Fallica G., Taibi E., Caruso M.

Department of Medical Oncology, Humanitas Centro Catanese di Oncologia, Catania, Italy

Pegfilgrastim is a pegylated long acting analogue of filgrastim administered once per chemotherapy cycle that makes possible to maintain chemotherapy dose intensity limiting severity and duration of neutropenia. This adverse effect can be severe and lead to discontinuation or delay of chemotherapy, reducing dose intensity and decreasing patient survival. However pegfilgrastim may induce bone pain in a 60-70% of patients, so effective preventive treatments for pain should be used. Unfortunately NSAIDs are sometimes the cause of gastrointestinal bleeding and so they are not desirables during breast adjuvant chemotherapy where the simultaneous use of high dose of steroideal anti-inflammatory is necessary. Conversely codeine and acetaminophen do not cause gastric and renal toxicity, and even at dose of 1.5 grams per day, for short periods, have negligible effect on hepatic metabolism. Aim of this open label randomized study was to compare pegfilgrastim induced bone pain incidence and its severity with (arm A) and without (arm B) prophylactic medication for pain based on codeine 30 mg/acetaminophen 500 mg TID from the second day until the seventh day from chemotherapy. Patients were eighty early breast cancer patients in adjuvant treatment with myelosuppressive chemotherapy (FAC-docetaxel, FEC-docetaxel, AC-docetaxel). Median age was 53 (range 26-73). PS ECOG was 0. The incidence of pain was significantly different: 70% (28 pts) in the arm B (without prophylactic medication) versus 50% (20 pts) in arm A with codeine/acetaminophen. Severe pain (5 to 7 in NRS pain rating scale) was also different: 25% (10 pts) in arm B versus 15% (6 pts) in arm A. Also, the duration of pain was different: 2.5 days without prophylactic medication versus 1.5 days with codeine/acetaminophen. Prophylactic medication with codeine 30 mg/acetaminophen 500 mg ter in die should be considered a valid option for patients to begin to treat with pegfilgrastim, because it can reduce the incidence, severity, and duration of pegfilgrastim induced bone pain and can improve the quality of care.

F51 ANALYSIS AND COMPARISON OF DATA RELATING TO OPIOID ORAL DRUGS USE ON THE WHOLE TERRITORY OF ITALY AND IN THREE REGIONS DURING 2009 AND 2010 FIRST SEMESTERS

Belfiore G.*, Gattaceca E.*, Condemi G.°, Tosolini F.^, Bellini G.^

**Associazione Abruzzese GIGI Ghirotti Onlus; °ASL Locri, ^Regione Friuli Venezia Giulia*

Italy is one of the worst countries in using analgesic narcotic drugs in the severe and middle pain.

So the Ministry of Health wanted to spur the use of these drugs with various initiatives to sanitary operators and finally in June 2009 introduced a law to simplify the prescription of these drugs (not-injective oppioid drugs especially).

This remarking study, after an international excursus and an observation of the Italian trend in the last years, where is remarkable a good tendency, but far from the European standards, observes the drug prescriptions on the whole territory of Italy and particularly on territory of Friuli Venezia Giulia (north Italy), Abruzzo (middle Italy) and Calabria (south Italy), comparing articulate data of the first six months of the year 2009 (before new law) with data of the first six months of the year 2010 (after the law).

We, especially, studied for each territory the parameters: cost, units, unitary cost, daily definite doses, for each therapeutic class, active principle and suministration way.

The most used drugs, in Italy, were codein + paracetamol and tramadol, both used for low-medium pain (over 70% of prescriptions).

The national trend is a growing use of these narcotic oral drugs, comparing the first semester of year 2009 with the first semester of year 2010. In facts, units increased of 927,355 (+18.33%);

The cost increased of euro 10,140.088 (+31.8%); the DDD increased of 2,423 (+17%).

Explications and articulate data for each region will be available in the extended version of the work

F52 APREPITANT IN THE PREVENTION OF ACUTE AND DELAYED CHEMOTHERAPY-INDUCED NAUSEA

AND VOMITING (CINV) IN ELDERLY PATIENTS WITH ADVANCED OVARIAN CANCER

Sciacca V.[2], Capparella V.[1], Rossi R.[2], Pace R.[1], Rauco A.M.[1], Pistillucci G.[2], Lugini A.[1]

[1]Medical Oncology, Ospedale Generale "San Camillo de Lellis", Rieti, Italy; [2]Medical Oncology, Ospedale "Santa Maria Goretti", Latina, Italy

Background and aims. Platinum/taxane doublets have long been considered the standard treatment regimen for advanced-stage ovarian cancer. Common side effects seen with the use of these drugs include gastrointestinal symptoms, myelosuppression and neurological toxicity. Nausea is the significant gastrointestinal adverse event because it results in a deterioration of patients performance status. What determines the need to stop treatment or to use lower drug dose intensity. Aprepitant, a neurokin-1 receptor antagonist, is a first-in-class agent approved for the prevention of acute and delayed chemotherapy-induced nausea and vomiting. Purpose of this study was to evaluate the efficacy of aprepitant in preventing nausea event preserving the quality of life of patients and the continuation of chemotherapy.

Methods. From August 2009 to November 2010, 15 patients (pts) with advanced ovarian cancer were included in the study. The patients received paclitaxel 175 mg/m^2 over 3 hours day 1, followed by carboplatin (area under the curve = 5) day 1, combined with a standard regimen of a dexamethasone and ondansetron, oral aprepitant (125 mg on day 1, then 80 mg once daily on days 2 and 3). QoL questionnaires were completed at baseline by 100% of patients.

Results. All patients were evaluable for the primary endpoint. Toxicity was grade 1 nausea (40%), grade 1 vomiting (5%). No patient reported a worsening of QoL to report the side effects of treatment.

Conclusions. Aprepitant has a significant role in the management of CINV, as it allows the majority of patients to complete their chemotherapies without significant morbidity.

F53 PROJECT CAPO: CONTINUITY OF CARE IN PALLIATIVE ONCOLOGY

Degiovanni D.[1], Ballarino P.[1], Gennaro G.[2], Giaretto L.[2], Botta M.[2]

[1]Unità di Cure Palliative, [2]Soc Oncologia, Casale Monferrato ASL AL

Introduction. The medical history of terminal illness interferes with daily life because of the duration and manifestations (psychomotor, social, and spiritual) of the disease. The range of these problems and their admixture recommends a comprehensive, holistic, as well as the complexity and fragility of the patient requires, multidimensional approach, exploring also the areas of needs that are often submerged, and the most likely potential one and highlights the functional capabilities residue. We can't say yet that the existing health care organization is always and easily accessible in the receiving care and treatment. The pathway to care for these patients can't be exclusive to one department, you can't think that assistance to cancer patient should be released in two distinct times (hospital and territory) and one that has to be active when the other one ends.

Methods. Thus the project CAPO was born (continuity of care palliative oncology), which is the realization of an integrated pathway between oncology and palliative care that will allow to optimize the framework of overall patient care in advanced stage of disease. The project involves the construction of an interdisciplinary pathway between oncologists and palliative care performers, and begins with the establishment of an integrated evaluation between these specialists.

Results. The project starts in a pilot phase from May to December 2009 and sees 50 patients enrolled in total: 28 (56%) were admitted to hospice and 22 (44%) were admitted to palliative home care. The sex of the patients is so distributed: 25 (50%) women and 25 (50%) men with a mean age of 71.3 years. The main diseases are: pleural mesothelioma 24%, lung cancer 18%, colorectal cancer 14% and 13% genitourinary cancer. The most represented symptoms are: nausea, dysphagia to solids and liquids, vomiting and respiratory symptoms such as cough and wheezing.

F54 IMPACT OF ANEMIA ON QUALITY OF LIFE IN ADVANCED CANCER: ONCOLOGY ISERNIA EXPERIENCE

Tomei F., Assalone P., Calista F., Traficante D., Di Lullo L.

ASReM U.O.C. di Oncologia F. Veneziale, Isernia

Background. The etiology of anemia in cancer is multifactorial. Anemia can be the result of either advanced disease or aggressive therapy. RBC transfusions and erythropoiesis-stimulating agents (ESAs) have provided treatment options for anemic patients. A decline in the subjective sense of wellbeing and functional impairment have been commonly identified as the quality of life domains most significantly disrupted by symptoms of anemia (fatigue, shortness of breath, weakness, chest pain headache and loss of appetite).

The aim of our study was to determine the impact of anemia on quality of life in patients with advanced cancer receiving chemotherapy.

Methods. From January 2010 to October 2010, 25 patients (14 males and 11 females) with advanced cancer, anemia (Hb level ≤12 g/dL) and Mini Mental Status score >19 were enrolled. Median age was 52.8 years; during chemotherapy 6 patients received RBC transfusions and 6 patients received erythropoiesis-stimulating agents (ESAs).

Choice of anemia treatment was based according to National and International Guidelines for anemia.

Quality of life was assessed using the Functional Assessment of Cancer Therapy-Anemia (FACT-An) questionnaire. The Fact-An questionnaire was self-completed by study patients on 3 occasions: baseline at study randomization before chemotherapy beginning, at the beginning of anemia treatment, when patients in the ESAs group achieved a hemoglobin concentration >11 g/dL and when patients in the transfusion group achieved a hemoglobin concentration >10 g/dL.

Results. Overall, 48% (12 of 25) of patients were evaluable while 13 of 25 patients didn't require anemia treatment during chemotherapy. In all evaluable patients changes in FACT-An score were correlated with hemoglobin levels. Increased hemoglobin levels improved FACT-An score.

Conclusions. According to literature data, our patients experiencing a decrease in their hemoglobin levels as result of chemotherapy benefited enormously from anemia treatment in terms of quality of life.

F55 PALLIATIVE DOMICILIARY TREATMENT IN THE VIBO VALENTIA PROVINCIAL HEALTHCARE ENTERPRISE

Gabrielli G., Spinoso A., Apriceno A., De Vita F., Arena M.G.

Division of Medical Oncology, Civil Hospital "Ignazio Toraldo", Azienda Sanitaria Provinciale di Vibo Valentia, Tropea,

Introduction. The Operative Unit of Medical Oncology of the Hospital of Tropea (VV) according to available region that provides funds for the activation of palliative care services has prepared a project for the palliative treatment at home.

Methods. In the three districts were organized under three Palliative Care Evaluation Unit, which had a specialist doctor as chief operating officer, already operating within the U.O. Medical Oncology, who had the task of coordinating the local activities. Other figures were triggered by medical and nursing services and other departments of the ASP (employees), after suitable training to the specific palliative care. These staffs carry out surveys and performance you need at home; the activities were carried out on time and paid to access the service.

Results. From September 2007 to December 2010 were treated 389 patients; mean age 73 years; 58.6 were females. Median survival: four months and twenty days. The diagnosis was: lung cancer 22%; colon cancer 15%; pancreas and biliary tract 13.6%; cancer of the prostate, bladder and kidney 12%; breast cancer 8%; gastric cancer 7.5%; gynecological 9%; others diseases (neoplastic and non) 13%.

Conclusions. In Calabria where the culture of palliative care is unfortunately still the pole and there are heavy economic difficulties for the re-entry plan and the block of new recruits, the Oncology Unit, in the absence of other significant initiatives in this regard by the government health authorities, has done its utmost to give rise to a service that would ensure palliative care to patients who no longer had the possibility of active treatment, and that such patients retain the most delicate moment in the course of the disease, the relationship with the team doctors who had treated (sometimes for several years); the activity has received numerous certificates of appreciation from the users and has enabled the U.O. to ensure, in almost all cases, a service that covers all the clinical course of disease (from diagnosis leading to death). This service is also offered as a reference for all the sick of the area needing treatment, it is palliative home care for patients previously followed in other places outside the territory of the ASP of oncology.

F56 INTEGRATION HOSPITAL/TERRITORY IN THE MANAGEMENT OF CRITICAL CANCER PATIENTS

Larizza E., Dilallo C., Pellachin S., Trecca R.

SoSD Oncologia Medica DH, P.O. Birago di Vische/Amedeo di Savoia, SL TO2 Nord, Torino

The Oncology Unit Birago di Vische made, throughout 2010, a project of integration hospital/territory to improve the quality of care for cancer patients in critical stage.

Participation in the meeting takes place following the proposal of the patient's medical oncologist, asking if he is available for interview integrated between physician teams (general medicine physician, medical oncologists, nurses, family members and caregivers).

Were carried out regular meetings, scheduled once a month for a total of 25 matches.

The time duration of the meetings has never been fixed, the average duration was one hour, but there were some meetings that have passed a hour and a half.

During the meetings were discussed the main problems related not only to treatment but to the real needs of the patient and family too; the interesting aspect of this project was the sharing of communication resources as effective means of comparison, depth and quality of therapeutic care.

A very large amount of time was spent listening to the needs, questions and observations of the patients. The results were very good: the patients had a higher compliance to therapy and a greater determination to address the criticality of the disease, the family has felt supported and protected by the team physician and has improved the approach and sensitivity to the patient. The team members have found in treating their union more professional and human resources as well as a deep spiritual satisfaction.

Session G • Genitourinary tumours

G1* INT70/09 PHASE II STUDY OF PAZOPANIB (PZP) MONOTHERAPY FOR PATIENTS (PTS) WITH RELAPSED/REFRACTORY UROTHELIAL CANCER (UC): UPDATED RESULTS OF A PROOF-OF-CONCEPT TRIAL (NCT01031875)

Necchi A.[1], Nicolai N.[2], Ortega C.[3], Sava T.[4], Sacco C.[5], Messina C.[6], Crippa F.[7], Morosi C.[8], Zaffaroni N.[9], Gianni A.M.[1,10], Salvioni R.[2]

[1]Medical Oncology, [2]Urology, [7]Nuclear Medicine, [8]Radiology, [9]Experimental Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan (IT); [3]Medical Oncology, Institute for Cancer Research and Treatment, Candiolo, Turin (IT); [4]Medical Oncology, University Hospital of Verona-Borgo Trento (IT); [5]Medical Oncology, Ospedale S. Maria Misericordia, Udine (IT); [6]Medical Oncology, Ospedali Riuniti di Bergamo, Bergamo (IT): [10]University of Milan School of Medicine, Milan (IT)

Background. Discouraging results have been reported with salvage therapies (Rx) in relapsed/refractory UC. In 2nd-line, median PFS and OS approximate 3 and 6 months, respectively, with a dramatic fall beyond 2nd-line. On 10/2010 we reported encouraging early results of a phase II trial with PZP. An update of the trial is presented.

Methods. Eligibility included histologically-confirmed UC failing ≥1 CDDP-based Rx for metastatic disease (perioperative Rx excluded). Daily PZP 800 mg until disease progression or unacceptable toxicity was planned. Both CT and PET/CT scan were set at baseline and q4 weeks thereafter. An optimal 2-stage design was applied with a full enrollment of 41 pts. RECIST v.1.1 response-rate was the primary endpoint.

Results. Thirty-six patients were enrolled from 02/10 to 03/11. Median age was 64 yrs (42-79). Thirteen patients (36%) had UC of the upper urinary tract and 23 a bladder primary. Median number of prior cytotoxic agents was 3 (2-8), of prior Rx lines was 2 (1-4), of prior platinum-based cycles was 5 (2-13). Ten patients had received RT. Thirty patients (83%) had visceral metastases. Median ECOG PS was 1 (0-2). Four patients (11%) had a confirmed RECIST-defined partial response (PR), 26 had a stable disease (83% clinical benefit). Nineteen patients (53%) had a necrotic evolution of multiple metastases and/or a decreased SUV at PET consistent with PR. Of the 34/36 pts having 2 mos minimum follow-up, median PFS and OS were 3 mos (1-11) and 6 mos (2-11), respectively. G3 hypertension occurred in 2 pts, G1-2 asthenia in 13, diarrhoea in 5.

Conclusions. This is the first report of an active and potentially effective targeted drug in UC. Though the PR-rate by RECIST is low, half of pts had a densitometric/metabolic response, the majority had a clinical benefit and PFS-rate is very promising. Results highlight the need for new response criteria of angiogenesis inhibitors. Final efficacy and safety outcomes with biomarker analysis will be available in 09/2011.

G2* IS PROGRESSION-FREE SURVIVAL (PFS) AN ADEQUATE SURROGATE ENDPOINT FOR OVERALL SURVIVAL (OS) IN THE 1ST-LINE TREATMENT OF ADVANCED RENAL CELL CARCINOMA (RCC)? CORRELATION AND POWER ANALYSIS OF RANDOMIZED CLINICAL TRIALS (RCTS)

Bria E.[1], Giannarelli D.[2], Massari F.[1], Cognetti F.[3], Tortora G.[1], Milella M.[5]

[1]U.O.C. Oncologia Medica dU, Azienda Ospedaliera Universitaria Integrata, Verona, Italy; [2]Biostatistics, Regina Elena National Cancer Institute, Roma, Italy; [3]Medical Oncology, Regina Elena National Cancer Institute, Roma, Italy

Background. Targeted agents (TAs) have been introduced in the treatment of advanced RCC mostly on the basis of PFS results. Although large retrospective non-randomized series suggest that PFS may be considered a reliable intermediate endpoint for OS with TAs (Heng Cancer, 2010), a formal analysis of correlation, surrogacy testing, and validation of such hypothesis is presently lacking.

Methods. RCTs evaluating the efficacy of TA as 1st-line treatment for advanced RCC were considered eligible. PFS/OS hazard ratios and response/disease control rates (ORR, DCR) were extracted from papers/updated presentations. Correlation analyses between efficacy (PFS) and activity (ORR/DCR) parameters and OS rates according to parametric (Pearson's r) and non-parametric (Spearman's Rho and Kendall's Tau) coefficients (with 95% CI) were performed at 3, 6, 9, and 12 months in order to avoid lead-time biases. Regression analysis (parametric R^2) was performed at the best performing time-point and a power-analysis-model, in order to determine the patients' sample necessary to determine 3%, 5% and 10% OS gain, was developed.

Results. Six RCTs (4096 patients) were gathered. No significant correlation was found between PFS and OS HRs (Pearson 0.37, p = 0.46). The best parametric coefficient was determined between 9 months PFS/OS. A significant correlation was also found between DCR, but not ORR, and OS. 9-mo correlations between PFS, DCR and OS are shown in the table:

Sample	Outcome	Correlation coefficient (p value)		
		Pearson	Rho	Tau
Overall	PFS	0.76 (p = 0.004)	0.94 (p = 0.002)	0.85 (p = 0.0002)
	DCR	0.63 (p = 0.04)	0.23 (p = 0.47)	0.11 (p = 0.71)
TA arm	PFS	0.87 (p = 0.02)	1.00 (p = 0.025)	1.00 (p = 0.0089)
	DCR	0.96 (p = 0.007)	0.82 (p = 0.10)	0.73 (p = 0.12)
Control arm	PFS	0.70 (p = 0.12)	0.86 (p = 0.05)	0.78 (p = 0.044)
	DCR	0.93 (p = 0.02)	0.60 (p = 0.23)	0.40 (p = 0.46)

The regression equation in the TA arm sample was y = 51.7226 + 0.5290X [R^2 0.761, p (intercept) = 0.017, p (slope) = 0.023]; based on this model, the demonstration of a 9-mo PFS absolute difference of 6%, 10% and 20% (corresponding to a 9-mo OS benefit of 3%, 5% and 10%) would require 2250, 750 and 190 patients, respectively.

Conclusions. Although individual patient data analysis for Prentice's criteria is needed for definitive confirmation, PFS may be considered an acceptable intermediate endpoint for ultimate survival benefit in the context of TA for 1st-line treatment of advanced RCC; the strongly significant correlation between DCR and OS deserves further investigation.

G3* META-ANALYSIS OF RANDOMIZED TRIALS (RCTs) EXPLORING THE EFFICACY OF ADJUVANT CYTOKINES (CK) OR VACCINES (VAX) OR OTHER

TREATMENTS (CHEMOTHERAPY, RADIOTHERAPY) AFTER SURGERY FOR RENAL CELL CARCINOMA (RCC)

Massari F.[1], Bria E.[1], Giannarelli D.[2], Milella M.[3], Cognetti F.[3], Tortora G.[1], Pappagallo G.[4], Porta C.[5]

[1]U.O.C. Oncologia Medica dU, Azienda Ospedaliera Universitaria Integrata, Verona, Italy; [2]Biostatistics, Regina Elena National Cancer Institute, Roma, Italy; [3]Medical Oncology, Regina Elena National Cancer Institute, Roma, Italy; [4]Epidemiologia-Sperimentazioni Cliniche, Ospedale Civile, Mirano (VE); [5]Oncologia Medica, Fondazione IRCCS Policlinico San Matteo, Pavia

Background. Adjuvant treatments have failed to provide a clear survival improvement after nephrectomy for localized RCC. While waiting for data from ongoing trials with anti-angiogenic agents and for the validation of recently suggested genomic profiles (high angiogenesis and cell-mediated factors versus high immune response, cell cycle and invasion factors) to stratify patients' prognosis (Rini B, ASCO 2010), we used a meta-analytical approach to explore whether CK, VAX, or other may influence patients' outcomes differently.

Methods. The objective was to determine whether significant interactions ('quantitative': diamonds on the same side of the plot; 'qualitative': diamonds on opposite sides) exist according to treatment (CK versus VAX versus other), in the context of a literature-based meta-analysis. Primary selected endpoint was 5-yr relapse-free survival (RFS); secondary endpoints were 5- and 2-yr overall survival (OS), and 2-year RFS. Event-based relative risk ratios (RRs) with 95% confidence intervals (CI) were extracted and cumulated according to a random-effect model from papers/presentation. Testing for heterogeneity was performed as well.

Results. Eleven trials (2,956 pts) were gathered and were evaluable for the primary outcome. A significant interaction ('quantitative' for CK versus other; 'qualitative' for VAX versus CK or other) according to treatment was found for 5-yr RFS, which is shown in the following Table:

	Overall	CK	VAX	Other
HR (95% CI)	1.12 (0.98, 1.27)	1.12 (0.98, 1.29)	0.91 (0.50, 1.66)	1.23 (0.64, 1.35)
p value	0.088	0.085	0.78	0.53
Het. (p)	0.023	0.76	0.04	0.05
Interaction (p)		0.035		

No significant interactions were found in 2-yr RFS (6 RCTs, 1,639 pts; RR 1.06, 95% CI 0.93, 1.20, p = 0.35; interaction p = 0.14), 5-yr OS (9 RCTs, 1,948 pts; RR 1.23, 95% CI 1.01, 1.50, p = 0.039; interaction p = 0.11), or 2-yr OS (6 RCTs, 1,209 pts; RR 1.11, 95% CI 0.91, 1.34, p = 0.28; interaction p = 0.58), with significant heterogeneity in all subgroups, with the exception of the CK sample.

Conclusions. The significant 'qualitative' interaction between VAX and CK is intriguing and suggests that VAX-based adjuvant strategies should be further investigated in the context of genomic-risk stratification of patients.

G4* EVEROLIMUS FOR COMPASSIONATE USE IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA (MRCC) PREVIOUSLY TREATED WITH VEGF (VASCULAR ENDOTHELIAL GROWTH FACTOR) INHIBITORS: THE LARGE ITALIAN EXPERIENCE

Bracarda S.[1], Hamzaj A.[2], Ishiwa O.[1], de Braud F.[3], Sisani M.[1], Lo Re G.[4], Basso U.[5], Fratino L.[6], Mazzanti R.[7], Sabbatini R.[8], Santini D.[9], Zustovich F.[5], Cartenì G.[10], Garassino M.[11], Zucali P.[12], Burattini L.[13], Milella M.[14], De Angelis V.[2] for the Everolimus Compassionate Use Italian Group

Medical Oncology Units of: [1]Arezzo; [2]Perugia; [3]European Oncological Institute, Milan; [4]Pordenone; [5]Padova; [6]Aviano; [7]Florence; [8]Modena; [9]Campus Biomedico, Roma; [10]Cardarelli, Napoli; [11]Fatebenefratelli, Milano; [12]Istituto Clinico Humanitas, Milano; [13]Ancona; [14]Regina Elena, Roma

Background. In the RECORD-1 phase III study, everolimus significantly improved progression-free survival (PFS) in patients with mRCC previously treated with sorafenib, sunitinib or both (4.9 versus 1.9 months). The recently presented data of the international expanded access program (ASCO GU, Symposium 2011, abstract 314) showed a similar safety profile and the possibility of a stable disease in 42% of the 605 evaluated patients. Here we present some preliminary data of the Italian experience with everolimus for compassionate use in mRCC.

Material and methods. Data of mRCC patients treated with everolimus, 10 mg initial daily dose, as compassionate use in Italian centers after failing previous treatments with VEGF inhibitors, from July 2008 were collected and analyzed. Patients could have clear or non-clear cell histology and should not be eligible for the concomitant expanded access program with the same drug.

Results. Preliminary data relate to 123 cases (median age 62 years, range 33-82; male/female ratio: 71/29/%; clear cell: 90.3%; median number of previous treatments 2). Most frequently reported grade 3 treatment related adverse events (AE) were anemia (15.4%), fatigue (5.7%), stomatitis (4.9%), hypertriglyceridemia (2.4%), hyperglycemia (2.4%), and infection (2.4%). Grade 3 non-infectious pneumonitis was reported in 1.6%. Hyperglycemia and anemia (each 0.8%) were the only grade 4 AEs reported. Median treatment duration was 5.3 months, with 8.1% of treated cases achieving a partial response and 40.6% a stable disease (intention to treat analysis, disease control rate 48.7%).

Conclusions. Also in this negatively selected population everolimus showed a good tolerability profile and the possibility of a disease control.

G5* NATURAL HISTORY OF MALIGNANT BONE DISEASE IN RENAL CANCER: RESULTS OF AN ITALIAN "BONE METASTASES" SURVEY

Santini D.[1], Procopio G.[2], Barni S.[3], Fontana A.[4], Berruti A.[5], Berardi R.[6], Ortega C.[7], Ibrahim T.[8], Cartenì G.[9], Bracarda S.[10]

[1]Oncologia Medica, Università Campus Bio-Medico, Roma; [2]Oncologia Medica, Fondazione IRCCS, Istituto Nazionale dei tumori, Milano; [3]Oncologia Medica, Azienda Ospedaliera Treviglio-Caravaggio, Treviglio (BG); [4]Oncologia Medica, Università di Pisa, Pisa; [5]Oncologia Medica, Università di Torino, Torino; [6]Oncologia Medica, Clinica di Oncologia Medica, A.O. Ospedali

Riuniti, Università Politecnica delle Marche, Ancona; [7]Divisione Universitaria di Oncologia Medica ed Ematologia, Istituto per la Ricerca e la Cura del Cancro (IRCC), Candiolo (TO); [8]Centro di Osteo-Oncologia, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Meldola (FC); [9]Oncologia Medica, Azienda Ospedaliera "Antonio Cardarelli", Napoli; [10]Oncologia Medica, Ospedale "S. Donato", Arezzo

Introduction. Bone metastases are an emerging clinical problem in renal cancer patients probably related to survival increase. There are few data in literature about the natural history of bone disease in renal cancer. We report the preliminary data of a large Italian multicenter survey.

Methods. 284 renal cancer patients with evidence of bone metastases have been included in the study at the moment of abstract submission. All patients were dead due to cancer at the moment of the study inclusion. Clinico-pathological data, data on survival and Skeletal Related Events (SRE) data and skeletal related therapies have been collected in a master data base and statistically analyzed.

Results. 202 males/82 females; median age: 63 (16-87); patients with bone metastases at the moment of renal cancer diagnosis: 31.5%; patients with single bone metastasis: 33%; lytic type: 78.6%, mixed: 13.6%, blastic: 7.8%. Sites: spine (71%), pelvis (35%), long bones (32%), other (15%). Median VAS pain at diagnosis: 4 (0-8), maximum pain: 7 (0-10). Median time to bone metastases: 8 months (0-288) (all patients); 25 months (1-288) (patients without bone metastases at diagnosis). Patients with at least 1 SRE: 68.3%. Types of SREs: pathologic fracture (12.8%), radiotherapy (63.2%), spinal compression (6.9%), bone surgery (14.5%), hypercalcaemia (2.6%). Median number of SRE for patient: 1 (0-4). Median time to first SRE: 1 (0-72), to second SRE: 3 (0-113), to third SRE: 8 (1-60). Median survival after bone met diagnosis: 12 (1-178). Median survival after first SRE: 10 (0-144). Median survival in patients with at least one SRE: 14 (1-178); median survival in patients without SREs: 9 (0-62).

Conclusions. Complete results of statistical analysis will be presented during the meeting. The present survey is the largest descriptive study concerning the natural history of bone disease in renal cancer patients.

G6* OVERALL SURVIVAL (OS) IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA (MRCC) TREATED WITH TARGETED THERAPIES (TTs): RESULTS OF A LARGE EXPERIENCE

Procopio G.[1], Verzoni E.[1], Iacovelli R.[2], Guadalupi V.[1], Gelsomino F.[1], Nicolai N.[3], Buzzoni R.[1]

[1]Medical Oncology Unit, Fondazione IRCCS, Istituto Nazionale Tumori, Milan; [2]Department of Oncology, Sapienza University of Rome; [3]Urology Unit, Fondazione IRCCS, Istituto Nazionale Tumori, Milan

Introduction. TTs are the standard treatment for mRCC. This study was performed to assess the OS in a consecutive series of mRCC patients receiving TTs.

Methods. Baseline characteristics and outcomes of 310 patients affected by mRCC receiving TTs were collected from the database of Istituto Nazionale Tumori of Milan. The main characteristics of patients were: ECOG PS 0/1/2 168 (54%)/123 (40%)/19 (6%); clear-cell histology 268 (86%); previous nephrectomy 273 (88%). According to Motzer criteria 32% of patients showed low risk, 47% intermediate risk and 21% had poor prognosis. Overall, 163 (53%) patients received one TT, 113 (36%), 30 (10%) and 4 (1%) received 2, 3 and 4 TTs, respectively. Altogether, 233 (75%) patients received sorafenib, 172 (55%) sunitinib, 32 (10%) a bevacizumab regimen and 20 (7%) other TTs. The uni- and multi-variate analyses for OS were carried out by means of Cox proportional hazard regression analysis.

Results. At a median follow-up of 37 months, 179 patients (57%) had died. The median overall survival (mOS) was 22 months and the 5-year OS was 23.4% without any statistical difference as regards the sequence used (Su/So vs So/Su) (HR 0.70; 95% CI: 0.40-1.23; p = 0.388 in the multivariate analysis). In patients receiving a bevacizumab regimen as first-line, no differences in OS were reported as compared to Su and/or So used sequentially (HR 0.85; 95% CI: 0.55-1.30; p = 0.675). These results were confirmed in the univariate analysis (Su/So vs So/Su) (HR 0.69; 95% CI: 0.41-1.16; p = 0.212) and bevacizumab vs Su and/or So (HR 0.77; 95% CI: 0.51-1.17; p = 0.212). According to Motzer criteria the median and 5-year OS were 43 months and 42.8%, 21 months and 15.9% and 8 months in low, intermediate risk and in high risk respectively.

Conclusions. These efficacy data suggest that TTs improve mOS in mRCC without a statistical difference when using different sequences of TTs. No cross-resistance between TTs was documented.

G7 A RETROSPECTIVE, MULTICENTER, ANALYSIS OF METASTATIC RENAL CELL CARCINOMA (MRCC) PATIENTS TREATED WITH EITHER SORAFENIB, AN mTOR INHIBITOR (mTORI) AND SUNITINIB, OR SUNITINIB, AN mTORI AND SORAFENIB

Paglino C.[a], Procopio G.[b], Sabbatini R.[c], Bellmunt J.[d], Schimidinger M.[e], Bearz A.[f], Bamias A.[g], Imarisio I.[a], Pedrazzoli P.[a], Porta C.[a]

[a]Medical Oncology, IRCCS San Matteo University Hospital Foundation, Pavia, Italy; [b]Department of Medical Oncology, Unit 2, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [c]Department of Oncology, Hematology and Respiratory Diseases, University of Modena and Reggio Emilia, Italy; [d]Medical Oncology Service, University Hospital del Mar, Barcelona, Spain; [e]Clinical Division of Oncology, Department of Medicine I and Cancer Center, Medical University of Vienna, Vienna, Austria; [f]IRCCS Oncology Reference Center, Aviano, Italy; [g]Department of Clinical Therapeutics, Athens University Medical School, Athens, Greece

Background. Since the approval of 3 multikinase and 2 mTOR inhibitors (mTORI), an increasing number of mRCC patients have been empirically treated with a sequential treatment approach. However, the optimal sequential use of all these agents has yet to be estabilished. The purpose of this retrospective analysis was to assess the clinical benefit of 2 different sequential approaches, i.e., sorafenib, an mTORI and sunitinib, or sunitinib, an mTORI and sorafenib.

Material and methods. This study was a retrospective analysis of 40 patients with mRCC treated between September 2005 and October 2010 at 6 European Centers. All patients were treated first-line with either sunitinib or sorafenib, followed by a second-line treatment with an mTORI (everolimus or temsirolimus),

and, upon further progression, with the other multikinase inhibitor (sorafenib or sunitinib).

Results. Twenty-six patients were treated with the sequence sorafenib-mTORI-sunitinib and 14 with the sequence sunitinib-mTORI-sorafenib. Baseline patient characteristics were similar between both populations in terms of age, ECOG performance status, Motzer's score, Fuhrman's grade, and presence of liver metastases. In the sunitinib-mTORI-sorafenib group, a higher incidence of non-clear cell mRCC was observed (5/14 vs 0/26 in the sorafenib-mTORI-sunitinib group). The actuarial overall median PFS (not including inter-treatment periods) in the sorafenib-mTORI-sunitinib group and in the sunitinib-mTORI-sorafenib group was 21.9 and 22.8 months, respectively (Log-rank test: p = 0.928). In the sorafenib-mTORI-sunitinib group patient experienced a median PFS of 11.7 months at first-line, 5.1 months at second-line, and 9.1 months at third-line, while in the sunitinib-mTORI-sorafenib group the first-, second- and third-line PFS was 14.4, 4.3 and 3.9 months, respectively.

Conclusions. Even though biased by its retrospective nature and small sample size, this study suggests the absence of significant differences, in terms of median PFS, between patients treated with the two sequential modality considered. In particular, it is possible to assume that patients may be sensitive again to a multikinase inhibitor after a second-line treatment with an mTORI. The results of ongoing prospective studies will help us to define the best treatment sequence.

G8 MANAGEMENT OF NEUTROPENIC GERM CELL TUMOUR PATIENTS RECEIVING CISPLATIN, ETOPOSIDE AND/OR BLEOMYCIN (PEB/PE): RESULTS FROM THE SCANNER SURVEY

Rosti G.[1], De Giorgi U.[2], Salvioni R.[3] on behalf of the Italian Germ cell cancer Group (IGG)

[1]Oncologia Medica, Ospedale Civile, Treviso; [2]Oncologia Medica, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), Meldola (FC); [3]Urologia, Istituto Nazionale Tumori, Milano

Background. In order to better understand the current clinical practice in a potentially curative setting, we conducted a national survey to describe the management of neutropenia in germ cell tumor (GCT) patients treated with cisplatin, etoposide with/without bleomycin (PEB/PE) (first-line therapy for advanced stage and adjuvant therapy for first stage) in Italian Oncology Units (IOU) from January 1 to September 30, 2010.

Methods. One hundred and thirty-two Italian oncologists were invited to participate in this survey. They represent the population of GCT-specialized physicians and were identified from physicians registered on the Italian Germ cell cancer Group (IGG) and most of the IOU from "Libro Bianco AIOM" registry. We distributed a structured questionnaire with 21 questions.

Results. Sixty-one of 132 (46%) physicians returned the questionnaire. Overall 480 GCT patients were referred to be treated with PEB/PE in these centers from January 1 to September 30, 2010. Two hundred and thirty-one patients (48%) received PEB/PE for metastatic disease, one hundred and ninety-five (41%) in adjuvant setting, 30 patients (6%) in both cases, data not reported in 524 of cases (5%). Ninety percent of IOU referred to have used granulocyte colony stimulating factors (G-CSF): in 32% of patients as primary prophylaxis, in 21% as secondary prophylaxis, in 13% as salvage therapy, in 13% multiple settings, 21% data not reported. In primary prophylaxis, daily G-CSF were referred to be the most frequently employed in 59% of cases and peg-filgrastim in 41%. In secondary prophylaxis, daily G-CSF were referred to be the most frequently employed in 70% of cases and peg-filgrastim in 30%. In salvage therapy, daily G-CSF were referred to be the most frequently employed in 86% of cases and peg-filgrastim in 14%. Fifty-four of 61 (89%) of IOU perceived a high impact of the dose-intensity of PEB on the overall survival of GCT patients. As reported by responders, the re-challenge of bleomycin (day 9 and 16 of PEB regimen) is not influenced by the grade of neutropenia, thrombocytopenia and anemia, in 52%, 48% and 72% of IOU, respectively.

Conclusions. According to Italian GCT-specialized oncologists, primary and secondary prophylaxes are largely employed for PEB/PE support in GCT patients in Italy. The maintenance of dose intensity is considered a high priority for these patients.

G9 BEVACIZUMAB AND WEEKLY DOCETAXEL IN PATIENTS WITH METASTATIC CASTRATE-RESISTANT PROSTATE CANCER PREVIOUSLY EXPOSED TO DOCETAXEL

Roviello G.[1], Petrioli R.[1], Pascucci A.[1], Francini E.[1], Francini F.[1], Bargagli G.[1], Conca R.[1], Martellucci I.[1], Miano S.T.[1], Licchetta A.[1], Chiriacò G.[1], Fiaschi A.I.[3], Manganelli A.[4], Ponchietti R.[5], Savelli V.[6], Tomao S.[7], Fiorentini G.[8], Francini G.[1]

[1]Medical Oncology, [2]Department of Odontostomatology and Maxillo-Facial Surgery, [3]Pharmacology Unit, [4]Urologic Surgery, [5]Genitourinary Unit, [6]General Surgery, University of Siena; [7]Department of Experimental Medicine, University of Roma "Sapienza"; [8]Oncology Unit, S. Giuseppe Hospital, AUSL11, Empoli, Italy

Background. Patients with castrate-resistant prostate cancer (CRPC) who progress after docetaxel (D) treatment may be considered for a second-line chemotherapy. In the hypothesis that the antiangiogenic agent bevacizumab (Bev) may overcome the resistance to D, we evaluated the activity and tolerability of D and Bev in patients with metastatic CRPC previously exposed to D.

Methods. Treatment consisted of D 30 mg/m^2 i.v. for four consecutive weekly administrations followed by a 2-week rest interval, in addition to Bev 5 mg/kg i.v. every 2 weeks. The chemotherapy was administered until disease progression or unacceptable toxicity, and for a maximum of 30 weekly D cycles.

Results. Forty-three patients were enrolled: a PSA response was observed in 27 patients (62.7%, 95% CI 0.41-0.91), and a palliative response was achieved in 31 patients (72.1%, 95% CI 0.48-1.02). After a median follow-up of 11.3 months, only five patients had died. The regimen was generally well tolerated: grade III neutropenia occurred in 8 patients, grade III anemia in 6 patients and grade III thrombocytopenia in 4 patients.

Conclusions. Weekly D + biweekly Bev seems to be an effective and well-tolerated treatment option for patients with metastatic CRPC previously exposed to D-based chemotherapy.

G10 EFFICACY OF ZOLEDRONIC ACID IN PATIENTS WITH RENAL CANCER METASTATIC TO BONE

Tonini G.[1], Lanzetta G.[2], Silvestris N.[3], Tanca F.[4], Mazzara C.[1], Virzi V.[1], Badalamenti G.[5], Luzi Fedeli S.[6], Adamo V.[7], Santini D.[1]

[1]Oncologia Medica, Università Campus Bio-Medico, Roma; [2]Unità funzionale di Oncologia, Gruppo INI, Divisione Grottaferrata, Roma; [3]Oncologia Medica, Istituto Tumori "Giovanni Paolo II", Bari; [4]Oncologia Medica, Azienda Ospedaliero-Universitaria di Cagliari, Presidio di Monserrato, Monserrato (Ca); [5]Oncologia Medica, Università di Palermo, Palermo; [6]Oncologia Medica, Azienda Ospedaliera "S. Salvatore", Pesaro; [7]Oncologia Medica e Terapie Integrate, Università di Messina, Messina

Introduction. Bone metastases are an emerging clinical problem in renal cancer patients probably related to survival increase. There are few data in literature about the role of BPs in the treatment of bone disease from colorectal cancer. We present the preliminary data of a large Italian multicenter retrospective analysis.

Methods. 284 renal cancer patients with evidence of bone metastases have been included in the study at the moment of abstract submission. Patients characteristics, skeletal related events (SRE) data and median survival after bone metastases appearance have been collected in a master data base and statistically analyzed. The primary efficacy endpoint was time to first SRE; secondary endpoint was median survival.

Results. A total of 284 patients have been included for zoledronic efficacy analysis. A total of 130 patients received zoledronic acid (4 mg) via a 15-minute infusion every 4 weeks until performance status worsening or death. 154 patients have been analysed as control group. The median time to first SRE in the whole population was 1 month (0-72). The median time to first SRE in the zoledronic treated patients was 3 months (0-101) compared with 1 month (0-22) in the control group ($p < 0.05$). The median survival after skeletal progression was 12 (1-178). The median survival in the zoledronic treated group was 15 months (2-120) compared with 7 months (1-178). ($p < 0.05$). Only 2 cases of ONJ have been diagnosed.

Conclusions. Complete results of statistical analysis will be presented during the meeting. The present analysis represents a confirmation, in clinical practice scenario, of zoledronic acid activity in bone metastases in renal cancer patients.

G11 VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) AND CHROMOGRANIN A (CGA): POSSIBLE NEW PREDICTIVE FACTORS IN THE TREATMENT OF ELDERLY HORMONE-REFRACTORY PROSTATE CANCER (HRPC) PATIENTS

Carreca I.*, Antista M.*, Bellomo F*., Pernice G.*, Condemi G.**

**Chair of Oncology and Oncogeriatric Unit, University of Palermo, Italy; ** Oncology Unit, General Hospital Locri (RC), Italy*

Background. Several prostate cancers show focal neuroendocrine (NE) spots at the immunohistochemical analysis. CgA seems to be frequently associated to NE phenotype both in tissue and in circulation. Furthermore, high CgA levels during complete androgen blockade (CAB) therapy play a role in worsening prognosis of HRPC. VEGF is produced by NE cells and can stimulate neoangiogenic response of epithelial prostatic tissue. VEGF expression in NE cells is correlated with clinical characteristics and disease-specific survival. Somatostatin analogues induce a decrease in plasma CgA and could have also anti-angiogenic activity by inhibition of VEGF, bFGF and GH/IGF-I axis.

Methods. Elderly patients, median age 75 (range 65-83), were selected for hormone-refractory disease, previously treated with CAB. Serum PSA and plasmatic CgA and VEGF were evaluated in all pts at baseline (T_0) and at 4 months (T_4) and 8 months (T_8) after therapy. Patients were treated with docetaxel 75 mg/m^2 every 3 weeks for 6 cycles and octreotide acetate 20 mg administered intramuscularly every 4 weeks until progression. Clinical and biochemical response, progression-free survival and toxicity were also evaluated. A correlation of basal CgA and VEGF with biochemical response, clinical response and clinical benefit was also investigated.

Results. Median duration of follow-up was 18 months (range 8-32). Patients evaluable for response were 22. PSA response rate (RR) was observed in 10/22 (45%); clinical objective RR was 33% (7/22). Clinical benefit was observed in 19/22 pts (86%). Only mild toxicities were observed in both groups. CgA and VEGF were both strongly reduced after therapy. Lower CgA values correlated with clinical benefit, lower VEGF values also correlated with biochemical and clinical response.

Conclusions. In this study we found a good tolerability and efficacy profile of a combination therapy with docetaxel and somatostatine analogue. The efficacy seems to be correlated with CgA and VEGF levels, suggesting the importance of the assessment of angiogenesis and NE differentiation for the management of HRPC elderly patients.

G12 DOES RESPONSE TO 1st-LINE TREATMENT WITH ANTI-VEGF RECEPTORS TYROSINE-KINASE INHIBITORS (TKIs) FOR ADVANCED RENAL CELL CARCINOMA (A-RCC) PREDICT OUTCOME? RETROSPECTIVE ANALYSIS OF A MONO-INSTITUTIONAL SERIES

La Russa F.[1], Maines F.[1], Massari F.[1], Bria E.[1], Sperduti I.[2], Sava T.[3], Molino A.[3], Cetto G.[4], Artibani W.[5], Martignoni G.[6], Tortora G.[1]

[1]Oncologia Medica dU, Azienda Ospedaliera Universitaria Integrata (AOUI), Verona, Italy; [2]Biostatistics, Regina Elena National Cancer Institute, Roma, Italy; [3]Oncologia Medica dO, [4]Medicina a Indirizzo Palliativo, [5]Urologia, [6]Anatomia Patologica, AOUI, Verona, Italy

Background. Agents targeting angiogenesis are dramatically changing the prognosis of patients (pts) affected by A-RCC. Nevertheless, it is still controversial which is the optimal upfront drug strategy and which predictors are able to tailor the appropriate treatment. In order to assess predictors for progression in the context of a mono-institutional series, a retrospective analysis was planned.

Methods. A-RCC pts referring to AOUI from January 2005 to April 2011, who received sunitinib (SU), sorafenib (SO) or preplanned sequential SU-SO were considered eligible. Descriptive statistics was adopted. Hazard ratios (HR) for progression-free and overall survival (PFS/OS) and the 95% confidence intervals (CI) were derived by using the Cox univariate model. A multivariate Cox proportional hazard model was developed. The Kaplan-Meier method was adopted for the survival estimation.

Table - G12

		PFS			OS		
		Median (95% CI)	p	1-yr (%)	Median (95% CI)	p	1-yr (%)
Response	Yes	16 (13-19)	<0.0001	77.6	n.r.	0.0009	94.7
	No	4 (3-6)		15.4	10 (8-12)		40.
MSKCC	Favourable	18 (3-34)	0.06	62.9	n.r.	0.04	100
Score	Intermediate	6 (4-9)		33.3	14 (4-23)		53.4
	Poor	3 (0-6)		14.3	11 (2-18)		47.6
Treatment	SU	9 (3-14)	0.34	41.2	29 (5-52)	0.20	60.7
	SO	6 (1-11)		36.5	15 (4-25)		57.1
	SU-SO	7 (5-8)		36.4	n.r.		71.1

Results. Sixty-five pts were gathered, as follows: male/female: 67.7%/32.3%; radical nephrectomy yes/no: 84.6%/15.3%; Fuhrman grading 1/2/3/4/5: 1.5%/15.4%/38.5%/18.5%/1.5%; MSKCC score favorable/ intermediate/poor: 21.5%/55.4%/12.3%; treatment SU/SO/SU-SO: 46.2%/26.2%/27.7%; >1 metastatic site yes/no: 29.2%/70.8%. At the multivariate analysis, response (HR 6.69, 95% CI 3.03-14.78, p <0.0001) and MSKCC score (HR 3.21, 95% CI 1.38-7.46, p = 0.007) were significantly independent predictors of PFS. Results are shown in the table.

Conclusions. Even if in the context of a retrospective series, the prognostic value of MSKCC score is confirmed; objective response seems to play as independent predictor for PFS as well. The current series does not have enough power to determine difference between VEGF-TKIs (SU vs SO) or strategies (i.e. sequential). Powered prospective trials and larger series are warranted.

G13 DOES QUALITY OF LIFE REALLY CHANGE DURING ACTIVE SURVEILLANCE? ONE YEAR FOLLOW-UP RESULTS OF PRIAS

Bellardita L.[1], Villani D.[1,5], Rancati T.[1], Marenghi C.[1], Procopio G.[2], Magnani C.[1], Avuzzi B.[1], Magnani T.[1], Salvioni R.[3], Nicolai N.[3], Villa S.[4], Valdagni R.[1,4]

[1]Prostate Program, Scientific Director's Office, [2]Department of Medical Oncology 2, [3]Department of Urology, [4]Department of Radiation Oncology 1, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milano; [5]Department of Psychology, Catholic University, Milan

Active Surveillance (AS) represents an attractive alternative to immediate treatment of low-risk indolent prostate cancer and implies medical (reduced risk of overtreatment and delay of radical therapies) as well as psychological advantages (distress related to treatment induced side effects).

The objective of this study is to monitor changes in quality of life (QoL) of patients on AS:

- at entrance in PRIAS (T0);
- 10 months after the diagnostic biopsy (T1);
- after the re-biopsy (T2).

Between September 2007 and January 2011, 100 patients entered in the PRIAS QoL study and 45 fully completed the T2 assessment. We evaluated QoL by measuring:

1. physical, social/family and emotional wellbeing (PWB, SWB, EWB) - functional assessment of cancer therapy;
2. adjustment to disease in terms of anxious preoccupation (AP) - MINI-mental adjustment to cancer;
3. mental-health status (only T0) - symptoms checklist 90.

Non parametric analyses showed that:

- AP significantly decreased (p = .004), in particular between T0 and T1 (p = .008);
- PWB did not significantly change (p = .798);
- SWB significantly decreased (p = .052), in particular between T0 and T1 (p = .014);
- EWB significantly increased (p = .003), in particular between T0 and T1 (p = .015).

Correlation analyses showed that:

- positive correlations exist between AP and mental health, in terms of interpersonal sensitivity (rho = 0.370), depression (rho = 0.431), anxiety (rho = 0.370), and hostility (rho = 0.426);
- negative correlations exist between EWB and interpersonal sensitivity (rho = -0.389), depression (rho = -0.463), anxiety (rho = -0.447), and hostility (rho = -0.354).

AS seems to be an adequate alternative to avoid overtreatment in terms of maintaining the patients' quality of life. Physical wellbeing does not decline, as patients do not experience side effects. Social wellbeing is high at the time of diagnosis and we could argue that its decrease is coherent with the reduction of patients' anxiety and need for support.

Patients with a not impaired mental health at entrance in AS present a better adjustment to cancer and a general wellbeing.

Acknowledgements to Fondazione Monzino Milan and Fondazione ProADAMO ONLUS.

G14 PILOT TRIAL OF CISPLATIN, 5-FLUOROURACIL AND A TAXANE (TPF) IN PATIENTS WITH ADVANCED SQUAMOUS-CELL CARCINOMA (SCC) OF THE PENIS: RESULTS FROM A SINGLE-INSTITUTION SERIES

Necchi A.[1], Nicolai N.[2], Colecchia M.[3], Catanzaro M.[2], Torelli T.[2], Biasoni D.[2], Stagni S.[2], Milani A.[2], Piva L.[2], Salvioni R.[2]

[1]Medical Oncology, [2]Urology, [3]Pathology, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan (IT)

Background. Patients with penile SCC having metastatic bilateral or pelvic nodes show an overall survival (OS) of 15% and less than 10%, respectively. We evaluated TPF in either neoadjuvant (NA), adjuvant (A) or metastatic (M) setting.

Methods. 3-4 courses of paclitaxel 120 mg/m^2 d1 or docetaxel 75 mg/m^2 d1 + cisplatin 75 mg/m^2 d1 + 5-FU 750 mg/m^2 96 hrs infusion from d1, q3wks were provided. Primary endpoint was progression-free survival (PFS). Immunostaining for p53, p16,

p63, EGFR, HER2/neu and mutational analysis of TP53 was planned.

Results. From 7/2004 to 03/2011, 40/46 evaluable pts were treated. Grade ≥3 hematologic toxicity was observed in 4 patients. Median PFS and OS on entire series were 6 (1-73) and 9.5 mos (1-73). Positive p53 staining significantly associated with better OS and PFS at univariate analysis (Logrank test p = 0.0421 and p = 0.0483).

Adjuvant setting: 17 pts (including 4 bilateral and 11 pelvic pN+) underwent adjuvant TPF. Median PFS and OS were 10 mos (1-73) and 13 mos (1-73). Ten pts (59%) were alive with 17 mos (1-73) of median follow-up.

Neoadjuvant setting: 16 pts with cN2/3 SCC were treated, either at diagnosis (11) or following recurrence after prior lymphadenectomy (5). Median PFS was 4 mos (1-46). Three pts achieved a complete response (CR) and 6 a partial response (PR, RR = 62%). OS was 5 mos (3-46). 9/16 pts underwent radical surgery. Three pathologic CR (27%) were achieved. Eight pts (50%) were alive after a median of 9 mos (3-46).

Metastatic setting: 7 pts were treated. Two had a PR and 1 a SD lasting a median of 5 mos (3-8), and all died of disease. Median PFS and OS were 2 mos (1-8) and 5 mos (2-12).

Conclusions. Perioperative TPF was effective in advanced penile SCC, deserving further investigation including earlier stages. Neoadjuvant TPF allowed to perform a radical surgery even in nodal relapses after prior intervention. Mature results on biomarkers will be available in September 2011.

G15 HEMATURIA IN ADVANCED BLADDER CANCER (BC): EFFICACY OF HYPOFRACTIONATED RADIOTHERAPY IN PATIENTS ADMITTED IN PALLIATIVE CARE UNITS (PCU)

Rozzi A.[1], Salerno M.[3], Bordin F.[5], Spigone B.[2], Nappa M.[2], Minniti G.[4], Nardoni C.[1], Corona M.[1], Falbo T.[6], Lanzetta G.[1]

[1]Clinical Oncology Unit, [2]Radiation Oncology Unit, Istituto Neurotraumatologico Italiano (INI) Grottaferrata, Grottaferrata (Rome); [3]Palliative Care Center "S. Antonio da Padova", Rome; [4]Radiation Oncology Department, S. Andrea Hospital, Rome; [5]Sue Ryder Foundation, Rome; [6]Experimental Medicine Department, University of Rome "La Sapienza", Rome

Background. Bleeding occurs in approximately 6%-10% of pts with advanced cancer. External-beam radiotherapy controls bleeding in up to 60% of cases of hematuria from bladder cancer (BC). In previous studies hypofractionated regimens for pts with bleeding from advanced BC demonstrated to be well tolerated and less distressing than more prolonged schedules.

Patients and methods. From January 2004 to September 2010 we consecutively recruited 33 pts with bleeding BC not amenable to surgical or radiotherapeutic intervention with radical intent and admitted into palliative care program. Characteristics of patients were as follows: M26:F7, median age 67 years (range 56-84 yrs), median KPS 40 (range 30-60). No patient was previously treated with radical pelvic radiotherapy or surgery. Before starting palliative radiotherapy 21 patients (64%) were requiring red blood (RBC) cells transfusions. Hypofractionated radiotherapy was planned to deliver a total of 21 Gy at 7 Gy per fraction. Patients were considered as responders if they had complete disappearance of visible hematuria (cleared hematuria). Moreover, we also evaluated the proportion of pts which continued to require transfusions after the completion of radiotherapy.

Results. All 33 patients completed hypofractionated radiotherapy: 20 patients (61%) had complete disappearance of haematuria. The median time to cleared haematuria was 11.2 days (range 7-32 days). Median survival was 49 days (range 23-123 days): only three patients with cleared haematuria (15%) had recurrent vesical bleeding. Before the beginning of treatment 21 patients (65%) required RBC transfusions: after completion of radiotherapy only eight patients (24%) were still receiving RBC transfusions.

Conclusions. To our knowledge, this is the first experience which evaluated the role of hypofractionated radiotherapy for vesical bleeding in patients with end-stage BC. Hypofractionated radiotherapy had a clear positive impact on haematuria: 60% of patients were rendered haematuria-free and the vast majority of them maintained themselves cleared until death. Moreover, another positive finding emerged from our study was the less needing of RBC transfusions. Such results should enforce the collaboration among palliativists, radiotherapists and oncologists.

G16 AN INTENTION TO TREAT (ITT) EVALUATION OF DOCETAXEL CHEMOTHERAPY RECHALLENGE IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (mCRPC)

Sisani M.[1], Rossi M.[2], Galli L.[3], Pastina I.[4], Falcone A.[3], Hamzaj A.[2], Scali S.[1], De Angelis V.[2], Bracarda S.[1]

[1]Medical Oncology, Arezzo; [2]Medical Oncology, Perugia; [3]Medical Oncology, Pisa; [4]Medical Oncology, Grosseto

Background. Docetaxel-chemotherapy (DCT-CT) is the first-line standard of care for mCRPC. Because no data exist about the most appropriate treatment duration in responding patients, a matter of interest in mCRPC, we evaluated the possible advantages of a rechallenge chemotherapy approach.

Material and methods. From July 2000 to September 2010, all consecutive patients treated with docetaxel for mCRPC in our Institutions were evaluated for a possible rechallenge with DCT-CT. In non-progressing cases, DCT-CT was interrupted either because PSA decreased by at least 90% or after a minimum of 6 cycles in the case of a PSA plateau. Median time to definitive progression (TTDP, defined for this protocol as the interval between the first DCT-CT infusion and the first evidence of definitive biochemical or clinical progression during treatment), the primary endpoint of the study, was calculated for the entire treated population (responding and non-responding patients; intention to treat analysis: ITT).

Results. Data relate to 102 evaluated patients (median age 73 years, median Gleason score 8, median baseline PSA 55.3 ng/mL); 82/102 cases achieved at least a stable disease after a median treatment duration on the initial DCT-CT round of 5.0 months (range 0.6-15.5), for a disease control rate (DCR) of 80.4%. After a median off-treatment period of 6.5 mos (range 1.3-28.0) 74/82 responding cases underwent a second DCT-CT round because of a biochemical or clinical progression, and 37 responded (DCR 52.9%, median treatment duration 3.6 mos). After a further median off-treatment period of 4.8 mos, 31 patients underwent a third DCT-CT round and 12 responded (DCR 38.7%; median treatment duration 2.1 mos) with 8/10 starting, after a median off-treatment period of 4.2 mos, a fourth DCT-CT round (2 responders). The actual median TTDP for the entire study population (102 cases) is 16.4 months (range 0.9-56.8). Any increase in grade 3/4 toxicities was observed.

Conclusions. With a median overall ITT TTDP of 16.4 months, docetaxel rechallenge should be considered as a reasonable treatment option for mCRPC patients initially responding to DCT-CT. These results should be verified in controlled clinical trials.

G17 RATE OF COMPLETE REMISSION (CR) USING TWO SEQUENTIAL, DOSE-DENSE REGIMENS OF CISPLATIN, GEMCITABINE, AND PACLITAXEL (CGP) FOLLOWED BY M-VAC IN PATIENTS WITH METASTATIC BLADDER

Brighenti M.[1], Passalacqua R.[1], Potenzoni D.[2], Potenzoni M.[2], Donini M.[1], Liguigli W.[1], Poli R.[1], Benecchi L.[2], Lazzarelli S.[1], Panni S.[1]

[1]Istituti Ospitalieri, Cremona, Italy; [2]Divisione di Urologia, Fidenza, Parma, Italy

Background. MBC is a chemotherapy sensitive tumour. Currently, CGP and MVAC are the most active regimens. According to Norton and Simon hypothesis, the administration of two sequential non cross-resistant, dose-dense chemotherapy regimens may target different cancer cells, avoid drug resistance, improve response rate and CR.

Methods. Patients with histological diagnosis of mBC, PS 0-2 (ECOG), adequate organ function and no previous systemic regimens were treated with 4 cycles of CGP dose-dense (gemcitabine 1000 mg/m^2 d 1, paclitaxel 140 mg/m^2 d 1, cisplatin 70 mg/m^2 d 2 plus pegfilgrastim 6 mg on day 3, every 2 weeks) followed by 4 cycles of M-VAC (methotrexate 30 mg/m^2 d 1,vinblastine 3 mg/m^2 d 2, doxorubicin 30 mg/m^2 d 2, cisplatin 70 mg/m^2 d 2 plus pegfilgrastim 6 mg on day 3 every 2 weeks). All were evaluated with CT scan at the baseline, after 4 cycles, at the end of chemotherapy and then every 3 months for two years and 6 months thereafter. Metastatic sites included retroperitoneal nodes, lung, liver and bone.

Results. From January 2007, 21 consecutive pts followed in the same oncology institution were included, 19 were evaluable. Males were 80%; median age 66 years; median PS was 90 (60-100); Bajorin risk factors were 0 in 33%, 1 in 40%, 2 in 27%. All pts were hospitalized for three days and received chemotherapy with generous hydration and supportive therapy. After the first 4 cycles of CGP we observed 11.1% CR, 55.5% PR, 16.6% SD and 16.6% PD. With the 4 sequential cycles of M-VAC the response was enhanced in 33% of the patients with a global 32% of CR, 31% of PR, 11% of SD and 26% of PD. Main grade 3-4 toxicity included asthenia (33%), neutropenia (26%), febrile (6.6%), thrombocytopenia (6.6%) and mucositis (13.3%). All patients with RP recurred whereas 5/6 patients with CR maintained the NED status after 1+, 6+, 9, 12+, 13+, 25+.

Conclusions. The results of this trial confirm the Norton-Simon hypothesis also in patients with metastatic bladder cancer. The sequential use of this two dose-dense regimens was very active and a significant percentage of patients maintained a CR status. A longer follow-up is needed in order to see if some patients are cured.

G18 MULTIPLE RE-CHALLENGES (RECS) WITH DOCETAXEL (DOC) IN CASTRATION-RESISTANT PROSTATE CANCER (CRPC) PATIENTS (PTS): FEASIBILITY, CLINICAL OUTCOMES AND PREDICTIVE FACTORS OF RESPONSE

Caffo O.[1], Veccia A.[1], Brugnara S.[1], Caldara A.[1], Ferro A.[1], Frisinghelli M.[1], Murgia V.[1], Soini B.[1], Valduga F.[1], Pappagallo G.[2], Galligioni E.[1]

[1]Medical Oncology Department, Santa Chiara Hospital, Trento, Italy; [2]Oncology and Hematology Unit, Mirano, Italy

Background. ReC with DOC has emerged as a therapeutic option for patients with CRPC who respond to first-line docetaxel and then discontinue treatment without experiencing disease progression. The present study attempts to describe the feasibility and clinical outcomes of multiple ReCs and to analyse the predictive factors.

Material and methods. From March, 2002 to December, 2010, a consecutive series of 46 CRPC pts received at least one ReC after first-line DOC, for a total of 92 ReCs (median 2, range 1-7). ReCs consisted of 4-6 DOC cycles and were proposed until the appearance of a true resistance to DOC. For each ReC course, we recorded the following parameters: treatment schedule, estramustine use, previous PSA response, baseline parameters (haemoglobin, alkaline phosphatase, pain presence, ECOG), number of previous DOC courses, PSA kinetic parameters during both previous DOC course and treatment holiday, duration of treatment holiday before ReC. A binary logistic regression analysis was applied. Continuous variables were categorized by quartiles and chosen for the initial model after an univariate chi-square analysis.

Results. In 66% of 92 ReCs we observed a PSA reduction >50%. After a median follow-up of 25 mos, the median survival is 32 mos and the projected 2-year overall survival is 77.5%. The observed major toxicities were: grade 3 anemia (2%), grade 3 neutropenia (2%), and grade 3 sensitive neuropathy (2%); two patients developed deep vein thrombosis (4%). Having an interval log-PSA equal to or more than 0.62, an interval from the previous cycle equal to or more than 23 weeks, a response to the previous cycle resulted to be independently predictive of a response to ReC.

Conclusions. In our experience ReC appears to be a good option able to obtain further response. Response to the previous cycle, interval log-PSA ≥0.62 and the interval from the previous cycle of at least 23 weeks are factors able to identify the pts having more probabilities to respond to ReC.

G19 UPDATE MANAGEMENT OF GERM CELL TESTICULAR TUMOURS: 1980-2010

Pizzocaro G., Guarneri A.

Clinica Urologica II, Università degli Studi di Milano, Ospedale San Giuseppe, Milano

Today, approximately 95% of all patients with germ cell testicular tumours (GCTT) can be cured. Today goals are: to avoid unnecessary over treatment and to improve cure in high risk patients.

We reviewed 676 consecutive patients personally treated in the period 1980-2009: 501 for non seminomatous GCTT and 175 for pure seminoma.

At the beginning of these series, RPLND was performed in all clinical stages I, IIA and IIB non-seminoma and radiotherapy was given to pure seminoma, but improving CT scan, serum tumour markers and introducing PEB, chemotherapy became preferred for high risk patients and low risk could enter surveillance.

Time from orchiectomy to clinical evidence of first metastases in initially clinical stage I patients is different in relation to prevalent histology and natural histology: it is very short in rare, very aggressive corio-carcinoma; time is usually within 2 years for embryonal carcinoma (ECA) with elevated AFP, and is the most common non-seminomatous tumour.

On the other side, 5 years follow-up or more are necessary for yolk sac tumour, usually with elevated AFP and associated teratomas.

Teratomas are slow growing tumours, usually refractory to chemotherapy, with very late symptoms, when the mass becomes very large. Pure seminoma is a relatively slow growing tumour (6 years) but in few cases seminomas may behave as very aggressive tumour (bad seminoma), which produces high amounts of HCG and develops quickly large amounts of resistant metastases.

In conclusion, germ cell testicular tumours do have different histologies and different natural histories: they all must be recognised and appropriately treated. Standard pure seminoma can be fit for surveillance but bad seminoma does need aggressive treatment. Stage I embryonalcarcinoma can be treated with surveillance in good risk patients, and with adjuvant chemotherapy for high risks. Stage I yolk sac tumours do need radical surgery. Stage I teratoma is to be followed annually, to avoid late surprise.

G20 THE ANTICANCER mTOR-INHIBITOR TEMSIROLIMUS INDUCES CARDIAC DYSFUNCTION IN MICE

Tocchetti C.G.[1], Coppola C.[1], Quintavalle C.[2], Barbieri A.[1], Rea D.[1], Palma G.[1], Gala M.[1], Luciano A.[1], Giudice A.[1], Capasso I.[1], Arra C.[1], Iaffaioli R.V.[1], Condorelli G.[2], Maurea N.[1]

[1]National Cancer Institute, Sen. Pascale Foundation; [2]Federico II University, Naples, Italy

Purpose. The mTOR inhibitor temsirolimus is being evaluated for anticancer efficacy in hundreds of clinical trials and is approved for treatment of advanced renal cell carcinoma. The PI3K/Akt pathway converges on mTOR, which is a central regulator of cell growth, including cardiomyocyte growth. Here, we aim at assessing whether the anticancer mTOR-inhibitor temsirolimus affects cardiac function.

Methods. *In vivo* cardiac function was measured with left ventricular (LV) fractional shortening (FS) by M-mode echocardiography in sedated C57BL/6 mice (2-4 months old) at day 0, and after 2, 7, 14, 21 days from a single i.p. administration of temsirolimus (0.1mg/kg, a dose comparable with the one used to treat cancer in humans) or vehicle. Doxorubicin (Doxo, 2.17 mg/kg/day for 7 days) was used as a positive control. With speckle tracking echocardiography (ST) we also evaluated radial myocardial strain (%), a very sensitive parameter which can detect subtle changes in cardiac function.

Results. After 2 days, there was no change in FS with temsirolimus, but FS was already reduced with Doxo: 52±0.2%, p = .0000001 vs sham (60 ± 0.4%). FS was reduced only after 21 days in the temsirolimus group: 50±3%, p = .009 vs sham. Interestingly, with Speckle Tracking echocardiography we found that radial strain was already decreased at 7 days in the temsirolimus group: 42 ± 5%, p = .01 vs sham (59 ± 1%).

Conclusions. The mTOR inhibitor temsirolimus induces LV dysfunction in mice. Such dysfunction occurs later than the one observed with Doxo, but can be identified with speckle tracking echocardiography (reduction in myocardial strain) before a decrease in FS is observed with conventional echocardiography. The clear mechanisms of temsirolimus cardiotoxicity are to be elucidated in further experimental studies. We also plan to apply speckle tracking echocardiography to clinical studies, in order to evaluate the impact of early identification of temsirolimus cardiotoxicity in the treatment of renal cell carcinoma.

G21 PSA FLARE-UP AND DOCETAXEL TREATMENT IN CASTRATION-RESISTANT PROSTATE CANCER

Grillone F., Fortugno C., Burgio V., Tassone P., Tagliaferri P.

Medical Oncology Unit, Magna Græcia University and Tommaso Campanella Cancer Center, Catanzaro, Italy

Background. Docetaxel plus prednisone (DP) is the standard treatment for castration-resistant prostate cancer (CRPC). It is well known that in some patients a transient increase of serum PSA (PSA flare-up) occurs after the beginning of chemotherapy. It is, however, not clear to what extent it occurs and whether it is associated with a different patient outcome. We here in evaluated the occurrence of PSA flare-up in CRPC patients.

Materials and methods. A series of 41 consecutive CRPC patients previously treated with DP for at least 12 weeks (January 2006 to December 2010) were included in a retrospective evaluation. PSA flare-up was defined as an increase of PSA ≥2 ng/mL over pre-treatment levels 21 days after the beginning of treatment, followed by a decrease in PSA until the achievement of a PSA response according to PCWG2 criteria. Patients have been defined as PSA flare-up/responders (PSA/f-R) if they showed flare-up/response to the treatment, non PSA flare-up/ responders (PSA/nf-R), if they responded but did not show flare-up and non responders (PSA/nR).

Results. PSA flare-up was observed in 15 (36.5%) patients and lasted 3-16 weeks. All these patients demonstrated symptomatic relief and no radiological findings suggestive of disease progression. Overall RR was 75%. Progression-free survival was 7, 6 e 2 months and OS 24, 15 e 7.5 months respectively in PSA/f-R, PSA/nf-R e PSA/nR, without reaching statistical significance when PSA/f-R and PSA/nf-R were compared.

Conclusions. Our study demonstrates that PSA flare-up is a common event in DP treated CRPC patients and can last up to 16 weeks. This finding raises major concerns in assessing progression in patients showing a PSA increase but demonstrating a symptomatic relief after the beginning of DP treatment. Moreover, PSA flare-up might be associated with long-term benefit of treatment which needs to be investigated in a larger series.

G22 PHASE II CLINICAL TRIAL WITH PHARMACOKINETICS (PK) AND PHARMACODYNAMICS (PD) EVALUATION OF METRONOMIC ORAL VINORELBINE (V) AND DEXAMETHASONE (D) IN PATIENTS WITH ADVANCED CASTRATION RESISTANT PROSTATE CANCER (CRPC): FINAL CLINICAL RESULTS

Derosa L.[1], Galli L.[1], Fontana A.[1], Cianci C.[1], Marconcini R.[1], Ferrarini I.[1], Stasi I.[1], Biasco E.[1], Orlandi F.[1], Fontana E.[2], Safina V.[2], D'Arcangelo M.[2], Allegrini G.[3], Lucchesi S.[3], Di Desidero T.[4], Bocci G.[4], Falcone A.[1,5]

[1]Division of Medical Oncology 2, Azienda Ospedaliero-Universitaria Pisana, Istituto Toscano Tumori, Pisa, Italy; [2]Division of Medical Oncology, Azienda USL-6 of Livorno, Istituto Toscano Tumori, Italy; [3]Division of Medical Oncology 2, Azienda USL-5 of Pontedera, Istituto Toscano Tumori, Italy; [4]Division of Chemotherapy and Pharmacology, Department of Internal Medicine, [5]University of Pisa, Italy

Background. Metronomic oral V and D have demonstrated a significant antiangiogenic property in preclinical models and an interesting activity without relevant toxicity in clinical trials.

Methods. Advanced CRPC patients received continuous V, 30 mg po three times a week and D, 1 mg po daily. Primary endpoint: the percentage of patients free of progression at 12 weeks; secondary: toxicities (NCI-CTC), activity (PSA reduction ≥50%); objective responses (RECIST), PFS, OS, pharmacodynamics and pharmacokinetics.

Results. Overall, 41 patients have been enrolled. Main characteristics were: median age 75.5 years (59-86), median PS 1 (0-2), median baseline PSA level 652.38 ng/mL (3.56-9032.00); main sites of disease: bone 35 (85%), nodes 16 (39%), prostate 23 (56%), lung 1 (2.4%). Previous chemotherapy was administered in 38 patients (92%): 35 docetaxel, 4 metronomic oral cyclophosphamide, 8 mitoxantrone, 3 estramustine, 2 epirubicin and sorafenib, 1 VP-16, carboplatin, sunitinib and gefitinib. The median number of previous regimens was 2.5 (range 0-5). Three patients (7%) received metronomic oral V and D as first-line treatment due to inability to receive standard chemotherapy or patient's preference; 18 (44%) as second and 20 (49%) as subsequent lines. Forty patients were evaluable for toxicity and response. Median duration of study drugs administration was 170 days (range 28-545). The rate of patients free of progression at 3 months was 60%. Main toxicity was grade 3 anemia in 1 patient (2.5%). A confirmed PSA level decrease ≥50% was found in 14 patients (35%). Two out of 12 evaluable patients obtained a PR and 9 a SD. Median PFS and OS were 3.02 (95% CI 1.3-4.7) and 14.3 (95% CI 9.8-18.8) months, respectively. Plasma concentrations of V and 4-0-deacetyl-vinorelbine, its main metabolite, were not detectable from patients samples, suggesting a not direct cytotoxic activity on tumour cells.

Conclusions. Our metronomic treatment showed a comparable activity to other metronomic schedules in advanced CRPC. The toxicity profile was also very favourable. The evaluation of plasma levels of thrombospondin-1, VEGF and sVEGFR as potential surrogate marker of antiangiogenic activity is still ongoing.

G23 SUNITINIB INDUCED HUMORAL PATTERN OF PRIMARY ALDOSTERONISM IN ADVANCED RENAL CANCER PATIENTS

Gambini D., Rescaldani M.[1], Turolo L.[1], Bolla G.[1], Magrini F.[1], Sala C.[1], Tomirotti M.

Medical Oncology Unit, Fondazione Ca' Granda Ospedale Maggiore Policlinico, Milano; [1]Heart and Lung Department and Centro Fisiologia Clinica e Ipertensione, Università di Milano e Fondazione Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy

Background. Hypertension is a frequent adverse effect of treatment with angiogenesis inhibitors in malignancies. To evaluate the role of the renin-aldosterone system in the blood pressure (BP) increase, we assessed plasma renin activity (PRA) and aldosterone (Aldo) before and after treatment with sunitinib (S, schedule 4/2), a blocker of vascular endothelial growth factor (VEGF)-mediated signaling, in patients with metastatic renal cell carcinoma.

Methods. In 5 patients (age 56 ± 2 yrs, M/F 3/2, BMI 29 ± 2 kg/m^2, MDRD glomerular filtration rate = 64 ± 7 mL/min/1.73 m^2), 24-hour BP and heart rate (HR) were monitored, supine PRA and Aldo were measured and Aldo to renin ratio (ARR) was calculated at baseline, after the first cycle of sunitinib (50 mg/day for 4 weeks) and after 2 weeks recovery.

Results. The table shows means ± sem; *p <0.05 vs baseline.

	24 hr BP mmHg	24 hr HR bt/min	serum K+ mEq/L	PRA ng/mL/h	Aldo ng/dL	ARR
Baseline	119/80 ± 6/4	78 ± 4	4.7 ± 0.4	0.9 ± 0.4	6.9 ± 1.8	13 ± 5
Sunitinib	141/99 ± 6/4*	73 ± 3	4.4 ± 0.2	0.2 ± 0.1*	11.3 ± 3.5	73 ± 25*
Recovery	125/83 ± 6/3	81 ± 3	4.5 ± 0.2	0.6 ± 0.3	9.2 ± 3.2	19 ± 8

Renal function was unchanged during treatment. Overall, ARR was related to systolic and diastolic BP values (r = 0.68 and 0.60, respectively, p <0.05).

Conclusions. Hypertension induced by S treatment in neoplastic patients is associated with increased ARR; this humoral pattern of primary aldosteronism is reversed after S withdrawal.

G24 FOCUS ON THE CONTINUOUS ANDROGEN DEPRIVATION THERAPY (ADT) IN THE OLDER PATIENT WITH ADVANCED PROSTATE CANCER

Castagneto B., Barbieri V., Biganzoli L., Carreca I., Colloca G., Conati G., Cova D., Gambardella A., Monfardini S., Scandurra G., Stevani I., Condemi G. on behalf of the Tavolo di Lavoro AIOM Oncogeriatria

Background. A part of adverse effects like gynecomastia, loss of libido, vasomotor flushing, ADT was recently associated with sarcopenic obesity, insulin resistance, lipid alterations, diabetes, and heart diseases.

Aim. Given the increasing prevalence of both metabolic syndrome (MS) and prostate cancer during old age we focused on the complications of the ADT in the elderly patient with advanced prostate cancer. We planned to take in consideration the MS in the elderly patient in treatment with ADT as topic of interest of the AIOM Task Force on Geriatric Oncology.

Methods. We provided a focus on the relevant literature using the following PubMed search terms: prostate cancer, elderly, obesity, androgen deprivation therapy, insulin resistance, diabetes, heart disease, and lipids.

Results. The fat accumulation during the ADT is mostly subcutaneous than intra-abdominal (Figure 1), but, of note, the sarcopenic obesity is associated with postural instability in the elderly subjects. The increased incidence of osteoporosis can expose this older patients population to a major risk of skeletal complications.

As for metabolic changes, some of these (increase in total cholesterol, low density lipoprotein, and triglycerides) overlap with MS features, but, unlike the decreased high density lipoprotein cholesterol associated with MS, ADT is characterized by an increased of this lipoproteic fraction. Likewise MS, insulin resistance is a metabolic condition that accompanies ADT (Figure 2). Finally, although there is no significant evidence of greater cardiovascular mortality in the general population treated by ADT, this trend has been documented in the CaPSURE database for the patients older than 65 years.

Conclusions. In patients receiving ADT for prostate cancer we suppose that the elderly could be considered at particular risk for skeletal traumatic events in relation to sarcopenic obesity.

As a consequence of greater incidence of impaired glucose tolerance and cardiovascular comorbidity for this set of patients clinicians should take in consideration strategies to decrease the risk of diabetes and cardiovascular death.

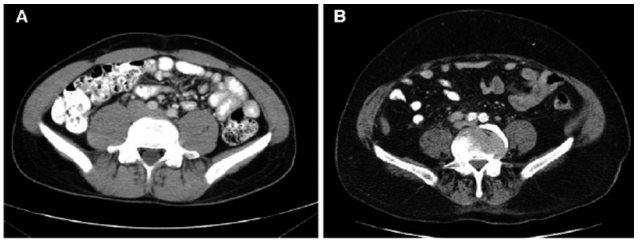


Figure 1

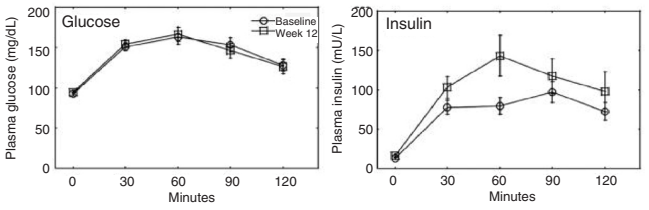


Figure 2

G25 PROSTATE CANCER UNITS IN EUROPE: SUGGESTING GENERAL RECOMMENDATIONS AND MANDATORY REQUIREMENTS

Valdagni R.[a,b], Albers P.[c], Bangma C.[d], Drudge-Coates L.[e], Magnani T.[b], Moynihan C.[f], Parker C.[g], Redmond K.[a], Sternberg C.N.[h], Denis L.[i], Costa A.[a]

[a]ESO, The European School of Oncology, Milan, Italy; [b]Prostate Program, Scientific Director's Office, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy; [c]Department of Urology, Heinrich Heine University, Düsseldorf, Germany; [d]Department of Urology, Erasmus Medical Center, Rotterdam, The Netherlands; [e]Department of Urology, King's College Hospital, London, United Kingdom; [f]The Academic Radiotherapy Unit, The Institute of Cancer Research and the Royal Marsden NHS Foundation Trust, Sutton & London, United Kingdom; [g]Academic Urology Unit, The Royal Marsden NHS Foundation Trust, Sutton, United Kingdom; [h]Department of Medical Oncology, San Camillo and Forlanini Hospitals, Rome, Italy; [i]Oncology Center Antwerp, Antwerp, Belgium

In prostate cancer (PC) multiple treatment/observational options are available. Multidisciplinary (MD) management facilitates high-quality medical procedures, collaboration among dedicated specialists, preventing and managing physical and emotional complications.

In 2010 the European School of Oncology identified general recommendations and mandatory requirements for the set-up of a PCU in a discussion paper (Eur J Cancer 47, 2011). A PCU should be referred ≥100 newly diagnosed PC cases each year. Therapeutic/observational protocols should be carried out under the direction of PCU. Data on diagnosis, treatment and follow-up should be recorded and available for audit once a year. A PCU should have a core team trained in PC who dedicates an agreed time to PCU and attends MD meetings (MDM): clinical director, ≥1 uro-pathologists, ≥2 urologists, ≥2 radiation oncologists, ≥1 medical oncologists, 1 nurse specialist in PC, ≥1 data managers, 1 professional responsible for monitoring the compilation of patient data. The PCU should have access to associated services and non-core personnel: ≥1 radiologists, ≥1 medical physicists, ≥2 radiation therapy technologists, ≥1 physiotherapists, ≥1 palliative care specialists, 1 clinical psychologist, 1 sexologist/andrologist, 1 geriatrician, ≥1 clinical trial coordinators, patient advocates.

Urologist, radiation oncologist and medical oncologist (if possible, a psychologist) should participate synchronously or in rapid succession in a weekly MD clinic. Advanced, recurrent or metastatic PC patients (pts) should be offered clinic every 2 weeks. PCU should also supervise follow-up. All treatment/observational options should be offered and the pt's right to information and self-determination ensured.

In weekly MDM min 90% PC cases should be discussed and decisions documented in charts.

PCU should possess or have access to all the technological equipment for imaging, radiotherapy, pathology.

PCU require to reorganize PC services, work-flow and attitudes but it should have a favorable economic impact and avoid multiple consultations and inappropriate treatments. Certification of a PCU should be considered the necessary step to ensure optimal treatment and care.

G26 RISK SHARING IN CANCER CARE: AN ITALIAN CANCER CENTER EXPERIENCE

Ragazzini A., Di Iorio V., Masini C., Marri M., Minguzzi M., Amadori D., Nanni O.

Istituto Scientifico Romagnolo per lo studio e la Cura dei Tumori - IRST, Meldola (FC)

Background. Economic sustainability of treatment is a problem for healthcare authorities and is linked to patients' rights to access treatment. The Italian Medicines Agency (AIFA), like other regulatory bodies, has developed reimbursement systems by risk sharing (RS) agreements with pharmaceutical companies.

Methods. This retrospective observational study evaluated anticancer drugs monitored by the AIFA RS program at the Cancer Institute of Romagna (IRST) for renal cell carcinoma patients treated with sunitinib or sorafenib. The audit's aims were to measure concordance between IRST computerized medical records and AIFA registers, to compare treated patients characteristics with those included in registry studies, and to evaluate the appropriateness of treatment prescription and disease re-evaluation timing on the basis of RS criteria. The RS program for the Italian National Health Service specified a 50% price reduction for the first 3 months of sunitinib and sorafenib, corresponding to 2 and 3 treatment cycles, respectively.

Results. Fifty-two patients received sunitinib and 24 sorafenib. Full concordance was observed between IRST electronic clinical forms and AIFA registers, in addition to high comparability between study populations, with the exception of a higher frequency of ECOG PS2 in IRST patients. Disease re-evaluation was performed in 39 (75%) patients treated with sunitinib; the first was carried out as planned for 30 patients and was delayed for 3 or 4 cycles in 9 patients, 4 of whom showed progression. For 17 (71%) patients treated with sorafenib, disease re-evaluation was performed as planned with the exception of 2 patients who progressed. If the 6 patients whose treatment was delayed had been evaluated on time, the Italian NHS would probably not have had to pay the full cost of drug prescriptions.

Conclusions. The clinical audit performed was an effective tool to monitor both the prescription process and the timing of disease restaging. Such a method could help to optimize the high cost of new cancer drugs and to facilitate a more accurate selection of candidate populations.

G27 THE OCCURRENCE OF HYPERLIPIDEMIA IN METASTATIC RENAL CELL CARCINOMA PATIENTS RECEIVING A SUNITINIB ADMINISTRATION

Baldazzi V., Tassi R., Lapini A.*, Carini M.*, Mazzanti R.

*2nd Medical Oncology Unit, *1st Urology Unit, Università degli Studi di Firenze, Azienda Ospedaliero-Universitaria Careggi, Firenze, Italy*

Introduction. Sunitinib malate is a tyrosine kinase inhibitor currently approved for the treatment of metastatic renal cell carcinoma (mRCC). Hyperlipidemia is not described among patients on sunitinib; however, it may induce an hypothyroid state, possibly causing an increase of serum lipids. Here we describe the occurrence of hypertriglyceridemia and hypercholesterolemia in patients receiving sunitinib for mRCC.

Patients and methods. Between July 2008 and November 2010, we prospectively evaluated serum triglycerides and cholesterol in 25 patients receiving sunitinib for mRCC (50 mg daily, according to classic 6-week schedule). Median patients age was 62.9 years. On average they received sunitinib for 7.2 cycles.

Serum lipids and thyroid function were measured before the beginning of treatment and at the end of each sunitinib ON period.

Results. At baseline median serum level of triglycerides was 141.78 mg/dL (± 22 mg/dL, 95% CI) and median cholesterol was 196.8 mg/dL (± 21.8 mg/dL, 95% CI). During sunitinib administration 16 patients (64%) presented an elevation of serum lipids. These abnormalities usually developed within 2 cycles (range 1-3 cycles).

In these patients, a maximum increase of median triglycerides and cholesterol of 160% and 36.1% respectively was observed. We did not observe a relationship between hyperlipidemia and hypothyroid state.

Considering all patients on sunitinib, at second cycle an increase from baseline of median serum triglycerides of 67.7% was observed, while at fourth it resulted of 46.9% and of 95.6% at sixth. Median serum cholesterol increased of 8.7% from baseline at second cycle, of 4.5% at fourth and 9.8% at sixth.

Conclusions. An elevation of serum triglycerides and cholesterol develops in patients on sunitinib.

This is a side effect described with mTOR inhibitors, other drugs prescribed sequentially to sunitinib in mRCC patients. Therefore, an elevation of triglycerides and cholesterol may persist for a long time in those patients. We recommend a careful monitoring of serum triglycerides and cholesterol among patients on sunitinib and more extensively during the treatment of mRCC

G28 BETWEEN CURRENT PRACTICE AND CLINICAL TRIALS RESULTS. THE EXPERIENCE FROM THE OSPEDALI RIUNITI OF BERGAMO

Bonomi L., Livraghi L., Messina C., Merelli B., Tondini C.

Oncologia Medica, Ospedali Riuniti, Bergamo, IT

Background. Sunitinib is a multi-targeted receptor inhibitor with activity in the treatment of advanced renal cell carcinoma (mRCC). We assessed efficacy and tolerability of sunitinib in an unselected population of mRCC seen at our center and compared our results with those in registrative clinical trial (RCT).

Patients and methods. We retrospectively reviewed data from all 54 consecutive with mRCC treated with sunitinib at our institution between June 2006 and June 2010.

Median age was 61 years; 83% had clear cell histology; 20% had progressed on prior treatment. The majority of patients had ECOG PS 0-1. 58% were MSKCC intermediate-risk and 16% poor-risk. Five patients had brain involvement. Most common comorbidities were hypertension (43%), gastric ulcer/GERD (11%), diabetes mellitus (11%), history of previous cancer (7%) and HBV/HCV infection (6%).

All patients were evaluable for toxicity and fifty for response. In RCT all were treatment naïve, had clear cell histology, ECOG PS 0-1 and no brain metastases. The majority of patients were at intermediate-risk, only 6% poor risk.

Results. Median follow-up time was 17.3 months. Objective response rate (ORR) 22%, 61% of patients had clinical benefit. Median progression-free survival (mPFS) was 11.6 months and median overall survival (mOS) has not been reached. In RCT ORR was 31%, mPFS 11 months and mOS 26.4 months.

33% of patients had dose reduction due to toxicity, 19% within the third cycle of treatment. Our patients' most common adverse events (AE) of all grades were fatigue (26%), neutropenia (20%), mucositis, hypothyroidism and thrombocytopenia (13%). Grade 3-4 neutropenia occurred in 9%. In RCT the incidence of AEs (all grades) was greater and dose reduction was applied in 50% of patients. Discontinuation of treatment due to AE was 2% in our study, 19% in RCT.

Conclusions. Our study confirms the activity of sunitinib for the treatment of m-RCC in a population of unselected patients seen at a general hospital, with slightly better results comparable with those reported in RCT.

G29 ACTIVITY OF NON PEGILATED LIPOSOMAL DOXORUBICIN IN COMBINATION WITH DOCETAXEL IN HORMONE-REFRACTORY PROSTATE CANCER (HRPC)

Rosselli M., Cammareri F.

Oncology Unit, Ospedale Regionale San Sebastiano Martire, Frascati (RM)

Purpose. Prostate cancer is one of the most common lethal tumours and the second cause of cancer mortality in males. It's initially treated by hormonal ablation with a median response duration of 12-16 months. Once prostate cancer has become refractory to hormonal therapy there are limiting options and in HRPC prognosis remains poor and new therapeutic strategies are therefore needed. Microtubule inhibitors have been a recent focus of investigation as chemotherapeutic agents in prostate cancer. In tissue culture, docetaxel appears to be the most active of these drugs and also anthracyclines were considered the gold therapy for patients with HRPC. Although no agents are approved for second-line therapy the present study was designed to assess the activity of non pegilated liposomal doxorubicin (Myocet®) in combination with docetaxel in this setting. Secondary objectives included treatment related toxicity, time to progression and overall survival.

Methods. We evaluated patients with HRPC, measurable disease and adequate cardiac function with left ventricular ejection fraction (LVEF) ≥50%.

Patients were treated with weekly intravenous non pegilated liposomal doxorubicin 20 mg/m^2 and docetaxel 30 mg/m^2 at day 1, 8, 15 every 28 days. Patients were treated for at least 6 cycles and first evaluation of response was done after 3 cycles.

Results. Fourteen patients were enrolled in the study. Median patient age was 77 years (range 65-88) and PS between 1 and 2. All patients have a metastatic disease (stage IV) at diagnosis with metastases localized mostly at bones, lung and nodes. Twelve patients were evaluable for response (completed at least 3 cycles) with 5 SD and 2 PR. Toxicity was generally mild with only one case of grade 4 neutropenia. There were no cases of heart failure or decrease of LVEF >10%.

Discussion. The responses seen in this population are very encouraging and suggest substantial durable activity for combination therapy with non pegilated liposomal doxorubicin and docetaxel for hormone refractory prostate cancer.

G30 TONGUE AS AN UNUSUAL METASTATIC SITE OF RENAL CARCINOMA AND ITS PROGNOSTIC VALUE

Fattoruso S.I.S.[1], Pacetti U.[1], Pagliuca G.[2], Gallo A.[2], Cardillo F.[1]

[1]Departmental Unit of Oncology, "A. Fiorini" Hospital, Terracina (Latina); [2]Operative Unit of Otolaryngology, University "La Sapienza" of Rome, Polo Pontino, Terracina (Latina)

Background. Renal carcinoma (RC) usually metastatizes to lung, thyroid, bone and liver; head and neck is described as an unusual site. Metastases to this region are a rare event. Renal cancer is the third most common tumour that metastatizes to head and neck region, following lung and breast.

Case report. A 72-year-old male, in April 2007, underwent a radical right nefrectomy for a renal clear cell carcinoma (G2 pT2; AJCC 2002).

In August 2008, because of right hand dysesthesia, he did a brain MR that showed a lesion of about 2 cm in the left parietal region. For this reason on 5 September 2008 the lesion was removed and the hystological examination testified it was a metastatic lesion of the clear cell renal carcinoma.

Surgery was followed by all brain irradiation for 30 Gy total dose. On December 2008 a restaging CT scan underlined some lung lesions. Therefore on 30 Dec 2008 he started treatment with sunitinib 50 mg/die for 4 weeeks q6 weeks. After just 3 cycles of sunitinib he gained a complete remission (CR) and he kept on untill 10 cycles.

After about 3 years of treatment the patient was very well, keeeping is complete remission on lung until new symptoms occurred.

In few days patient began symptomatic with sialhorrea and pain until a bleeding from the mouth started.

A laryngoscopy showed a neoplasm of the base of the tongue of about 2 cm.

On 30 April the neoplasm was resected and the pathological examination showed a metastatic lesion with clear cells according to the primary diagnosis of renal cancer. He died a month later.

Conclusions. From 1911 to nowadays literature data describe just 28 cases of tongue metastases and 60% of these is represented by Japanese cases (17 pts). Tongue metastatization is a late event that correlates with death regardless of clinical wellness.

G31 MORE THAN 20 YEARS OF OVERALL SURVIVAL IN A PATIENT WITH UNUSUAL ENDOTRACHEAL AND MAMMARY GLAND METASTASTIS OF RENAL CELL CARCINOMA TREATED WITH SORAFENIB AND SUNITINIB

Ciorra A.A.°, Sciacca V.°, Pistillucci G.°, Petricola F.°, Di Palma T.°, Calabretta F.°, Rossi R.°, Cirino C.°, Lugini A.*, D'Aprile M.°

*°Medical Oncology, "S.Maria Goretti" Hospital, Latina, Italy; *Medical Oncology, "S. Camillo De Lellis" Hospital, Rieti, Italy*

Introduction. Before 2005 the only options for the treatment of metastatic renal cell carcinoma (mRCC) were limited to the cytokines interleukin-2 and interferon-α with low rates of response and short survival of these patients. In the last 5 years several targeted therapies have become available for first- and second-line use as sorafenib (an oral multi-kinase inhibitor) and sunitinib (an oral multi-targeted receptor tyrosine kinase inhibitor) achieving improvement in median PFS (5.5 months and 11 months respectively).

Case report. We report the case of a 55-year-old woman affected by a metastatic renal cell carcinoma which developed unusual metastasis into the trachea and in the breast.

In August 1989 the patient underwent a left nephrectomy for a clear cell carcinoma with inferior vena cava involvement and submitted to post-operative chemotherapy with vinblastine for 13 months. Nine years later disease relapsed in the left lung and a solitary metastasis was surgically removed. The patient received immunotherapy with interferon-α for 6 months. In September 2002 a CT scan showed mediastinic nodal metastases that were treated with radiotherapy followed by gemcitabine and 5-fluorouracil for 12 cycles, obtaining a stable disease until January 2007 when appeared an endotracheal polypoid lesion histologically described as metastasis of clear cell carcinoma. We started sunitinib 50 mg/die continued until July 2009 when the patient referred a mobile nodule in her left breast. Histopathological findings showed a renal cell metastasis in the breast tissue: from August 2009 to January 2011 was administered sorafenib 800 mg/die without relevant toxicity. In February 2011 the patient presented progressive clinical impairment and died after 20 years from the initial diagnosis of advanced renal carcinoma.

Conclusions. This case report confirms that multidisciplinary approaches (surgery, radiotherapy and newer molecular-targeted agents) improve disease control in patients with mRCC without severe toxicities and in respect of quality of life.

Session H • Sarcoma, lymphoma, melanoma, brain tumours

H1* HODGKIN'S DISEASE AND HIV INFECTION (HD-HIV): PROGNOSTIC FACTORS IN 596 PATIENTS (PTS) WITHIN THE EUROPEAN GROUP FOR THE STUDY OF HIV AND TUMOURS (GECAT)

Spina M.[1], Ribera J.M.[2], Gabarre J.[3], Wyen C.[4], Montoto S.[5], Jaeger U.[6], Talamini R.[1], Re A.[7], Tirelli U.[1]

[1]National Cancer Institute, Aviano, Italy; [2]Hospital Universitari Germans Trias i Pujol, Badalona, Spain; [3]Hopital Pitié-Salpetrière, Paris, France; [4]University of Cologne, Köln, Germany; [5]Institute of Cancer for Medical Oncology Barts, London, UK; [6]University of Vienna, Vienna, Austria; [7]Spedali Civili, Brescia, Italy

Background. Hodgkin's disease (HD) is the most common non-AIDS defining tumour diagnosed in HIV setting. The introduction of highly active antiretroviral therapy (HAART) has opened a new prospective in the treatment of pts with HD-HIV as the better control of the underlying HIV infection allows the use of more aggressive chemotherapy regimens, including high dose chemotherapy. However, up to now prognostic factors on overall survival (OS) or time to treatment failure (TTF) have not been identified yet.

Methods. In order to identify prognostic factors, we analyze data on 596 pts with HD-HIV diagnosed and treated in 90 different Institutions from 6 European countries from October 1983 to March 2010. All factors were analyzed for OS and TTF.

Results. 86% of pts were male and the median CD4 cell count was 224/dL (range 3-1274); 52% of pts had mixed cellularity subtype, stages III-IV were diagnosed in 72% of cases and 55% of pts had extranodal involvement (bone marrow 35%, spleen 21%, liver 14%). Table 1 summarizes the results of multivariate analysis.

Table 1

Factors	Overall survival	Time to treatment failure
IPS ≤2	1	1
IPS >2	2.33 (1.61-3.39) p <0.0001	1.57 (1.09-2.26) p = 0.02
CD4 ≥200	1	1
CD4 <200	1.63 (1.16-2.29) p = 0.005	1.43 (1.02-2.01) p = 0.04
European score		
0	1	1
1	2.06 (1.40-3.02)	1.64 (1.17-2.30)
2	3.08 (2.13-4.45) p <0.001	2.31 (1.66-3.20) p <0.001

Conclusions. We identified a new "European Score" for HD-HIV able to predict different outcomes in these patients. This score should be considered for future prospective studies.

H2* A PRIMARY OBSERVATIONAL ITALIAN NEURO-ONCOLOGY STUDY: PROJECT OF EMILIA-ROMAGNA REGION ON NEURO-ONCOLOGY (PERNO)

Brandes A.A.[1], Baruzzi A.[2], Mazzocchi V.[1], Poggi R.[1], Pisanello A.[3], Marcello N.[3], Depenni R.[4], Valentini A.[5], Albani F.[2], Faedi M.[6], Guiducci G.[7], Urbini B.[8], Crisi G.[9], Dascola I.[10], Mucciarini C.[4], Cavanna L.[11], Dazzi C.[12], Franceschi E.[1]

[1]Department of Medical Oncology, Bellaria-Maggiore Hospitals, Azienda USL, Bologna; [2]Department of Neurological Sciences, University of Bologna; [3]Department of Neurology, Arcispedale S. Maria Nuova, Reggio Emilia; [4]Department of Medical Oncology, Modena University Hospital, Modena; [5]Department of Neurosurgery, Modena Hospital, Baggiovara; [6]Department of Medical Oncology, [7]Department of Neurosurgery, Bufalini Hospital, Cesena; [8]Department of Medical Oncology, Sant'Anna Hospital, Ferrara; [9]Department of Diagnostic Neuroradiology, [10]Department of Neurosurgery, Azienda Ospedaliero-Universitaria di Parma, Parma; [11]Department of Medical Oncology, Piacenza Hospital, Piacenza; [12]Department of Medical Oncology, Ravenna Hospital, Ravenna

Background. The Project of Emilia-Romagna Region on Neuro-Oncology (PERNO) is the first Italian prospectic observational population-based study in neuro-oncology. In January 2011 the first step of the project about GBM patients clinical observation and management registration in the Emilia-Romagna region was concluded. Approvals from local Ethical Committees were obtained by 8 participating centers. No previous similar data were available in Italy, so the data presented here address this issue for the first time.

Methods. From January 2009 to January 2011, 187 patients (pts) who met the following inclusion criteria were evaluated: age ≥18 years; PS 0-3; histologically confirmed GBM, resident in Emilia Romagna region. The data were prospectively collected.

Results. The observed occurrences of cancers were spread in all centres: 36.5% of pts was randomised in Bologna and 63.5% in the other areas of Emilia-Romagna Region. Conforming to the expected rates, from the analysis of the clinical variables we observed that the median age was 61.5, with a predominance of males (60%) and 46% of pts were over 70 years of age. In 42% of pts a total resection of the disease was achieved, while 46% and 12% of patients received partial resection or biopsy, respectively. Early neuroradiological control (CT/MRI) was performed in 74% of the pts, while the median time for radiotherapy initiation was 42 days. The pts allocated the following forms of post-surgical treatments: 75% temozolomide concurrent with radiotherapy, 18% radiotherapy alone, 4% chemotherapy alone and 3% did not receive any treatment; 19% were included in clinical trials approved by Ethical Committees. The overall survival rate at 24 months was 23%, while the median overall survival was 13 months (95% CI 11.4-14.6).

Conclusions. This study, the first in Italy regarding the neuro-oncology field, showed the treatment care of GBM pts and the outcomes in the modern era. Moreover, this project acts also as functionally platform for translational research studies and provides pts common data set for further studies on GBM.

H3* MANAGEMENT OF METASTATIC BRAIN DISEASE: MONO-INSTITUTIONAL EXPERIENCE

Urbini B.*, Nisi C.*, Giuliani J.*, Schirone A.*, Carandina I.*, Fainardi E.°, Ceruti S.°, Sarubbo S.§, Cavallo M.A.§, Api P.#, Scapoli D.*, Piva E.*, Frassoldati A.*

**U.O. Oncologia Clinica, °U.O. Neuroradiologia, §U.O. Neurochirurgia, #U.O. Radioterapia Oncologica, Azienda Ospedaliero-Universitaria Sant'Anna, Ferrara*

Background and purpose. Brain metastases (BM) are the most common intracranial tumour in adults. Available evidences suggest that survival is longer if BM are treated aggressively. In the present study we evaluate if prognostic factors such as age, ECOG performance status (PS), number of BM, recursive partitioning analysis (RPA), time to BM appearance, integrated approach (surgery or radiosurgery (SRS) followed by whole brain radiotherapy (WBRT) ± chemotherapy) affect survival (OS) from BM diagnosis in our patients.

Materials and methods. We retrospectively evaluated data from 271 consecutive BM patients treated at our institution from January 1998 to December 2009, of which a complete clinical history was available. An univariate analysis for each prognostic variable on OS was estimated according to the Kaplan-Meier method [statistical significance ($p < 0.05$) of differences evaluated by Logrank test].

Results. Among the 271 patients [172 male and 99 female, median age 63 years (range 29-88)] the most frequent primary tumours were: NSCLC (43.2%), SCLC (16.2%), breast cancer (13.7%) and melanoma (4.8%). Median time to BM appearance was 6 months (range 0-268). At the time of BM diagnosis, 191 patients had ECOG PS 0-1, 97 patients had 1 BM, 74 patients had 2 or 3 BM and 100 patients had multiple BM. The most of the patients was in RPA class I and II (12.1% and 58.3%, respectively). Integrated treatment was administered in 23 patients, 17 of which also received chemotherapy. Mean OS from BM diagnosis was 5.9 ± 0.4 months (NSCLC:6.6 ± 0.8, SCLC: 5.7 ± 1.3, breast cancer: 6.9 ± 1.6, melanoma: 3.3 ± 0.6 months). Univariate analysis for OS showed statistically significant differences for ECOG PS 0-1, RPA class I and integrated treatment (Table 1).

Conclusions. Although the management of BM remains challenging and often discouraging, a careful approach to identify patients suitable for aggressive treatment, on the basis of prognostic factors, may result in clinical benefit and prolonged survival. A multidisciplinary assessment is advised.

Table 1

	OS months (95% CI)	p value
ECOG PS		
0-1	6.9 (5.6-8.2)	<0.0001
2-3	3.6 (2.7-4.6)	
RPA		
I	8.2 (4.8-11.6)	0.001
II	6.7 (5.3-8.2)	
III	3.7 (2.7-4.6)	
Integrated vs single treatment		
Surgery + WBRT	17.3 (9.7-24.9)	<0.0001
SRS + WBRT	21.6 (7.6-35.6)	0.002
Surgery + WBRT + CT	18.9 (9.6-28.1)	0.001
SRS + WBRT + CT	24.2 (8.1-40.2)	0.002

H4* A SIMPLE PROGNOSTIC SCORING SYSTEM FOR NON-METASTATIC OSTEOSARCOMA OF THE EXTREMITY

Cesari M.[1], Serra M.[2], Alberghini M.[3], Ruggieri P.[4], Palmerini E.[1], Staals E.[4], Mercuri M.[4], Abate M.[1], Picci P.[2], Ferrari S[1].

[1]Chemotherapy Section, Rizzoli Orthopaedic Institute, Bologna; [2]Laboratory of Experimental Oncology, Rizzoli Orthopaedic Institute, Bologna; [3]Department of Surgical Pathology, Rizzoli Orthopaedic Institute, Bologna; [4]Department of Orthopaedic Surgery, Rizzoli Orthopaedic Institute, Bologna, Italy

Prognostic stratification of patients with non-metastatic osteosarcoma may improve the clinical management and the design of clinical trials.

Data from 773 patients, median age 15 years (3-40), treated at our Institute from 1983 to 2000 according to neoadjuvant chemotherapy with high-dose methotrexate, cisplatin, doxorubicin and ifosfamide were analyzed. After multivariate analysis including age, site, tumour volume (cut-off 200 mL), serum LDH and alkaline phosphatase (SAP), histology (osteoblastic and chondroblastic vs others), high LDH and SAP, osteoblastic and chondroblastic histotypes resulted independent prognostic factors of DFS. Patients were grouped according to a score from 0 (absence) to 3 (presence of one to 3 adverse factors). The scoring system was implemented by the addition of PgP expression and grade of chemotherapy-induced tumour necrosis.

A score of 0, 1, 2, 3 was given to 14%, 38%, 32% and 16% of patients respectively. 10-year DFS was 80% (95% CI 72-89) for score of 0, 58% (95% CI 52-64) for 1, 53% (95% CI 46-59) for 2 and 40% (95% CI 32-50) for 3 ($p = 0.001$).

PgP expression (available in 168 patients) identified patients with 100% probability of DFS (score of 0 and negative PgP) and patients with 18% (95% CI 52-64) DFS (score of 3 and positive PgP).

Good (GR) and poor responder (PR) patients had the same probability of DFS in case of score of 0 [GR 82% (95% CI 72-91), PR 79% (95% CI 65-93)] and score of 3 [GR 43% (95% CI 32-55) PR 36% (95% CI 21-51)]. Different probability of DFS in case of score of 1 [GR 64% (95% CI 57-72) PR 47% (95% CI 36-59)] and score of 2 [GR 63% (95% CI 55-71) PR 36% (95% CI 21-51)].

It is possible to stratify outcomes of patients with non-metastatic osteosarcoma of the extremity by means of a simple score based on easily available clinical parameters. This scoring system is worth to be validated on larger series.

H5* PROGNOSTIC FACTORS IN NEWLY DIAGNOSED GLIOBLASTOMA: HAVE WE MISSED GENDER?

Franceschi E.[1], Tosoni A.[1], Bartolini S.[1], Rimondini S.[1], Lombardo L.[1], Poggi R.[1], Dall'Occa P.[1], La Torre L.[1], Ermani M.[2], Brandes A.A.[1]

[1]Department of Medical Oncology, Bellaria-Maggiore Hospitals, Azienda USL, Bologna; [2]Neurosciences Department, Statistics and Informatics Unit, Azienda Ospedale-Università, Padova

Background. Following the EORTC/NCIC trial investigating temozolomide concurrent and adjuvant to radiotherapy, this regimen is considered standard treatment for newly diagnosed glioblastoma (GBM). However, although some studies report a marked difference between the incidence of grade 3/4 neutropenia in males and females, the role of gender as a prognostic factor has not yet been evaluated.

Methods. We analyzed the charts of all patients with newly diagnosed GBM treated in our department with the EORTC 22981/26981-NCIC trial in order to assess whether there is a correlation between gender and outcome.

Results. In the 105 GBM patients evaluated, median age 54 years (range 18-70); male/female: 63/42, resection was total in 49 and subtotal in 56; *MGMT* promoter was methylated in 45 (43%) and unmethylated in 60 (57%). Median time to disease progression was 11.5 (95% CI 9.4-13.6) months, and median sur-

vival (mOS) 18.7 (95% CI 16.8-20.7) months; *MGMT* methylation status (p = 0.04), gender (p = 0.03) and age (p = 0.02) significantly influenced survival. The interaction found between gender and *MGMT* methylation was significant, females harboring *MGMT* methylation surviving longer than other patients (*MGMT* methylated/unmethylated males and unmethylated females): mOS, 28.6 months (95% CI 24.7-32.5) and 18.2 months (95% CI 16.0-20.4), respectively (Table). Findings at multivariate analysis confirmed that age (p = 0.004) and interaction between gender and *MGMT* status (p = 0.008) significantly correlate with OS.

Conclusions. Since no biological or clinical explanations are available to explain the above findings, we advocate the inclusion of gender as a potential prognostic factor in future trials.

	mOS (months)	95% CI (months)
Overall	18.7	16.8-20.7
Male/MGMT methylated	17.7	14.2-21.3
Female/MGMT methylated	28.6	24.7-32.5
Male/MGMT unmethylated	18.2	14.1-22.4
Female/ GMT unmethylated	18.7	13.4-23.9

H6* EVALUATION OF CXCR3 AND CCR5 POLYMORPHISMS AND GENE-EXPRESSION AS PREDICTIVE BIOMARKERS OF CLINICAL RESPONSE TO ADOPTIVE THERAPY IN MELANOMA PATIENTS

Bedognetti D.[1-3], Spivey T.L.[1], Uccellini L.[1], Wang E.[1], Dudley M.E.[4], Ascierto M.L.[1], Sertoli M.R.[1-3], Marincola F.M.[1], Rosenberg S.A.[4]

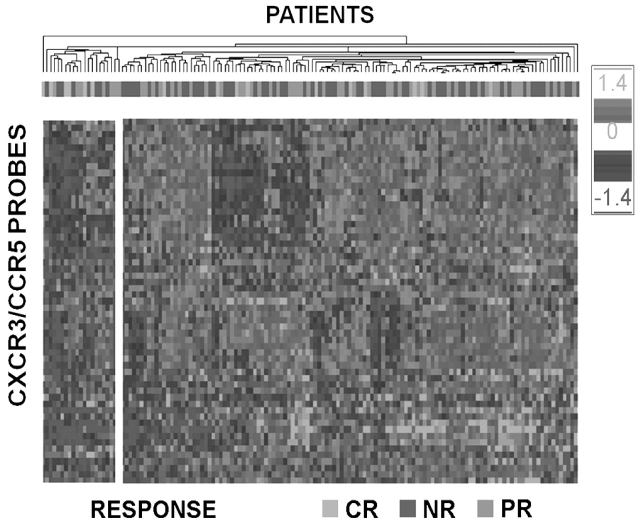
[1]Department of Transfusion Medicine, CC, CHI, National Institutes of Health, Bethesda, MD, USA; [2]Department of Oncology, Biology and Genetics, Department of Internal Medicine, University of Genoa, Italy; [3]Department of Medical Oncology, National Cancer Research Institute of Genoa, Italy; [4]Surgery Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA

Background. Adoptive cell therapy induces objective responses in approximately 50% of patients with metastatic melanoma. The recruitment of T lymphocytes through CXCR3 and CCR5-ligand chemokines is critical for the development of immune-mediated rejection. A common single nucleotide polymorphism of CXCR3 (rs2280964) has been associated with variation in chemotactic activity. CCR5 polymorphism Δ32 (a deletion of 32 bases encoding a protein not expressed on cell surface), has been recently correlated with poor prognosis in metastatic melanoma patients. We postulated that polymorphisms of CXCR3 and CCR5 genes may influence the migration of tumour-infiltrating lymphocytes (TIL) on tumour site and, eventually, the tumour regression.

Methods. One-hundred and forty-two TIL samples, belonging to 142 melanoma patients enrolled in consecutive adoptive therapy trials, were evaluated. Genotyping (rs2280964 and Δ32 mutation) was performed by sequencing. Gene-expression profiling of infused TIL was assessed by Affymetrix Human Gene ST 1.0 array (CXCR3, 27 probes; CCR5, 30 probes). DNA/RNA data were correlated with each other and with clinical response.

Results. Surprisingly, CCR5Δ32 carriers (n = 25) had a better overall response (OR: CR, complete remission or PR, partial remission) compared to wildtype patients (OR: 68% vs 46%, respectively, p <0.05). The under-expression of CXCR3 and CCR5 genes was independently correlated with CR (p <0.05). Interestingly, the co-underexpression of both genes was even more accurate in the prediction of CR: 29% (12/41) in CXCR3CCR5-low group compared to 4% (4/101) in the other patients (p <0.0001). Moreover, the protein-prediction-model was also predictive of OR: 64% (30/47) in CXCR3CCR5-low group and 43% (41/95) in the other patients (p <0.05). In this model CCR5Δ32 carriers with high CCR5 and low CXCR3 transcript levels were included on the CXCR3CCR5-low group. The protein-prediction model was validated by flow-cytometric analysis.

Conclusions. CCR5/CXCR3 transcript under-expression in TIL is associated with CR. The protein-prediction model suggests also a correlation with OR. This unexpected result allows to generate new hypotheses on the role of these pathways in the modulation of stimulatory or regulatory mechanisms in different conditions.



Self organizing heat map based on CXCR3 and CCR5 probes. In the left-square: low CXCR3CCR5 cluster enriched in CR (p = 0.0002).

H7 PHASE II STUDY OF INTRATHECAL LONG ACTING LIPOSOMAL CYTARABINE (DEPOCYTE®) IN THE PROPHYLAXIS OF LYMPHOMATOUS MENINGITIS IN HIV-RELATED NON-HODGKIN'S LYMPHOMA

Spina M.[1], Martellotta F.[1], Berretta M.[1], Zanet E.[1], Lleshi A.[1], Canzonieri V.[2], Bulian P.[3], Bibas M.[4], Antinori A.[4], Uziel L.[5], Manna A.[6], Carbone A.[2], Tirelli U.[1]

[1]Division of Medical Oncology A, National Cancer Institute, Aviano, Italy; [2]Division of Pathology, [3]Clinical and Experimental Unit of Hematology-Oncology, National Cancer Institute, Aviano, Italy; [4]Division of Infectious Diseases, Istituto Lazzaro Spallanzani, Rome, Italy; [5]Division of Medical Oncology, San Paolo Hospital, Milan, Italy; [6]Division of Medical Oncology, Sant'Andrea Hospital, La Spezia, Italy

Background. Around 5% of patients (pts) with aggressive NHL develop central nervous system (CNS) progression or relapse during their disease. Patients with HIV-related NHL often develop CNS progression despite use of adequate prophylaxis. Li-

posomal cytarabine has shown a significant activity in lymphomatous meningitis but there are limited data in prophylactic setting.

Methods. Since May 2006, we are running a prospective phase II study of intrathecal liposomal cytarabine (Depocyte®) dosed 50 mg in 48 pts with HIV-NHL aiming to evaluate feasibility and activity of this drug in preventing lymphomatous meningitis.

Results. Forty-two pts were males and median age was 44 years (range 18-69). Histological NHL subtype was: in 47% diffuse large B-cell (DLBC) NHL and 40% Burkitt NHL. Stage III-IV was diagnosed in 80% of pts and 68% of DLBC were age-adjusted IPI 2 or more. Extranodal involvement was diagnosed in 70% of pts (gastrointestinal 30%, bone 27%, spleen 10%, liver 22%, bone marrow 17%). Liposomal cytarabine was well tolerated with headache grade I to III being the most frequent side effect in only 32% of patients. Less common toxicity (all grade I) included cortical changes (4%), fever (2%), vomiting (2%), hypertension (2%), chills (2%). With a median follow-up of 15.5 months only one pt (2%) with Burkitt lymphoma developed combined systemic and meningeal relapse. Moreover, in our prior experience, we used methotrexate as practical use in 426 HIV-NHL with a meningeal progression or relapse of 14% ($p = 0.09$). Use of liposomal formulation allowed to significantly reduce the number of lumbar injections in comparison with standard schedules (approximately of 50%) with improvement of pts' quality of life and with reduction of professional exposure risk for health care staff.

Discussion. In this first prospective study on prophylaxis of lymphomatous meningitis in HIV-NHL reported in literature, liposomal cytarabine seems safe and active and reduces of approximately 50% the number of lumbar punctures and exposure risk for health staff as well.

H8 SPECTRUM AND PREVALENCE OF SOMATIC MUTATION IN *BRAF* AND *NRAS* GENES AMONG PRIMARY MELANOMAS AND THEIR METASTASES AT DIFFERENT ANATOMICAL SITES

Colombino M.[1], Capone M.[2], Maio M.[3], De Giorgi V.[4], Massi D.[5], Lissia A.[6], Cossu A.[6], Rubino C.[7], Muggiano A.[8], Staibano S.[9], Nappi O.[10], Pagani E.[11], Botti G.[2], Caracò C.[2], Mozzillo N.[2], Manca A.[1], Sini M.C.[1], The Southern Italy Cooperative Oncology Group (SICOG), The Italian Melanoma Intergroup (IMI), Ascierto P.A.[2], Palmieri G.[1]

[1]Istituto Chimica Biomolecolare, CNR, Sassari; [2]Istituto Nazionale Tumori Fondazione Pascale, Napoli; [3]Oncologia, Università di Siena; [4]Dipartimento Scienze Dermatologiche, Università di Firenze; [5]Istituto Anatomia Patologica, Università di Firenze; [6]Servizio di Anatomia Patologica, Azienda Ospedaliero-Universitaria, Sassari; [7]Chirurgia Plastica, Università di Sassari; [8]Ospedale Oncologico Businco, Cagliari; [9]Dipartimento di Scienze Biomorfologiche e Funzionali, Università Federico II di Napoli; [10]Servizio di Anatomia Patologica, Ospedale Cardarelli, Napoli; [11]Istituto Dermatologico dell'Immacolata, Roma, Italy

Background. Mutations of *NRAS* and *BRAF* genes have been identified with high frequency in nevi, cutaneous melanomas, and melanoma metastases. Prevalence of such mutations during the disease progression phases and among the different types of metastasis remains inconclusive. The present study attempts to clarify the frequency of *NRAS* and *BRAF* mutations in primary tumours and synchronous or asynchronous metastases from same patients.

Methods. Paired samples of microdissected invasive primary melanomas (n = 73) and corresponding metastases (n = 164) underwent mutation analysis by automated DNA sequencing. Secondary lesions were from: regional (RN; n = 49) or distant (DN; n = 16) lymph nodes; skin not beyond (loco-regional skin, LS; n = 16) or beyond (distant skin, DS; n = 18) the regional nodes; visceral (VM; n = 22) or brain (BM; n = 44) metastatic sites. Collection and analysis of samples is still ongoing.

Results. To date, mutations were identified in 44/73 (60%) primary melanomas [31 (42%) in *BRAF* gene and 13 (18%) in *NRAS* gene], 43/65 (66%) lymph node metastases [32 (49%) in *BRAF* and 11 (17%) in *NRAS*], 21/34 (62%) subcutaneous metastases [13 (38%) in *BRAF* and 8 (24%) in *NRAS*], 13/22 (59%) visceral metastases [10 (45%) in *BRAF* and 3 (14%) in *NRAS*], and 31/44 (70%) brain metastases [21 (48%) in *BRAF* and 10 (23%) in *NRAS*]. Overall, a slight and not significant increase in mutation frequency after progression from primary melanoma was observed in our series [108/164 (66%) mutated metastases: 76 (46%) in *BRAF* and 32 (20%) in *NRAS*]. The only significant differences were found for subcutaneous metastases: a) DS presented a significantly higher mutation frequency than LS (78% vs 44); and b) a discontinuous pattern of *BRAF*/*NRAS* mutations was detected when comparing LS/DS lesions with primary melanomas. These latter findings suggest that independent subclones may have been generated; however, such discrepancies have been found at significant levels for skin metastases only (few differences in distribution of mutations were detected when comparing other metastatic sites with primary melanomas).

Conclusions. Although mutation analyses are being increased, our results may indeed provide further clues about the impact of *NRAS* and *BRAF* mutations among the different stages of melanoma progression.

H9 FIRST GENOMIC STUDY WITH MASSIVELY PARALLEL SEQUENCING IN GASTROINTESTINAL STROMAL TUMOUR KIT/PDGRFA WILD TYPE (WT-GIST) IDENTIFIED MUTATIONS IN SDHA GENE

Pantaleo M.A.[1,2], Indio V.[2,3], Astolfi A.[2], Paterini P.[2], Formica S.[2], Casadio R.[3], Martelli P.L.[3], Maleddu A.[1], Nannini M.[1], Pallotti M.[1], Mandrioli A.[1], Lolli C.[1], Saponara M.[1], Di Battista M.[4], Gatto L.[1], Santini D.[5], Catena F.[6], Dei Tos A.P.[7], Biasco G.[1,2]

[1]Department of Hematology and Oncological Sciences "L. A. Seragnoli", [2]Interdepartmental Centre for Cancer Research "G. Prodi", [3]Biocomputing Group, Bologna Computational Biology Network, University of Bologna, Bologna, Italy; [4]Department of Medical Oncology, Bellaria-Maggiore Hospital, Azienda USL of Bologna, Bologna, Italy; [5]Pathology Unit, [6]Emergency Surgery and Transplant Department, S. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy; [7]Azienda ULSS 9 Treviso, Treviso, Italy

Background. Massively parallel RNA sequencing allows to discover novel single nucleotide variants and to identify new potential target genes in rare diseases, such as WT-GISTs.

Methods. Whole transcriptome RNA sequencing was performed by Illumina GAIIx system using a 75 bases paired-end strategy on tumour samples of two young adult patients affected by gastric WT GISTs. Sequences were aligned with BWA against exon + junction references. SNVmix2 was used for SNP calling,

identifying 2045 and 1780 coding non-synonymous novel single nucleotide variants (SNVs) in the two patients respectively. After checking misalignments by SAMTools, the variants were filtered to increase SNPcall confidence: SNVs with quality read score >30 (error probability of 0.1%), total coverage >40, and ratio between coverage of alterate base and total coverage >0.3 were labeled high confidence. Single point mutations were translated at the protein level and their likelihood of being disease-associated was computed with SNPs&GO and confirmed with Sanger sequencing.

Results. Mutations in SDHA (succinate-dehydrogenase subunit A) were highlighted commonly in both patients as disease-associated variants. Interestingly these mutations promote protein destabilization such as in the FAD binding domain. The results are also confirmed with protein structure computational analysis. Sanger sequencing on both tumour and peripheral blood (PB) samples found that one patient tumour DNA was homozygous for an exon 9 **p.S384X** nonsense mutation; the second patient was a compound heterozygote for a germinal exon 2 **p.R31X** nonsense mutation and a somatic exon 13 **p.R589W** missense mutation. Additional 8 tumours and 6 PB DNA from 14 sporadic WT GISTs patients were sequenced, finding 6 other SDHA mutations in 3 patients. Globally we found 9 different mutations in 5 out of 16 patients (31%).

Conclusions. Massively parallel RNA sequencing, followed by data analysis, identified novel mutations in WT GIST. Among these, mutations in SDHA gene seem to be relevant for disease development and treatment targeting.

H10 TEMOZOLOMIDE (TMZ) MAINTENANCE AFTER POSTOPERATIVE TMZ PLUS RADIOTHERAPY (RT) IN PRIMARY BRAIN CANCER: A RETROSPECTIVE ANALYSIS

D'Auria G.[1], Fabbri M.A.[1], Sperduti I.[2], Mansueto G.[3], Fariello A.M.[3], Gamucci T.[3], Battista M.[4], Loffreda M.[5], Pompei L.[5], Moscetti L.[1]

[1]Medical Oncology, Ospedale Belcolle, Viterbo; [2]Biostatistics Unit, Regina Elena Institute, Rome; [3]Medical Oncology, [4]Radiotherapy, Ospedale SS Trinità, Sora; [5]Radiotherapy, Ospedale Belcolle, Viterbo

Purpose. To evaluate the efficacy and toxicity of the maintenance TMZ in patients affected by primary brain cancer previously treated with post-operative TMZ + RT, a systematic review of the clinical chart of two oncologic centers was undertaken.

Patients and methods. Ninety-nine patients were detected. Main characteristics were as follows: median age 62 years (range 28-80); M/F: 58/41; PS 0/1: 92 pts; complete resection: 75; subtotal resection: 20, biopsy only: 4. The median dose of RT was 60 Gy. All the patients received concomitant TMZ at 75 mg/m^2 during RT. Maintenance therapy with TMZ was given to non progressive pts, starting 6 weeks after TMZ + RT, at the dose of 150 mg/m^2 for the 1st cycle and 200 mg/m^2 q 4 weeks d 1-5 for subsequent cycles and continued until disease progression or intolerance.

Results. The overall response rate (ORR) after CT + RT was 16% (PR+CR) and a stable disease (SD) was observed in 66% of pts. Maintenance TMZ was given to 78% of patients. The median number of cycles administered was 6 (range 1-25). Maintenance treatment was well tolerated. Major hematologic toxicities include: grade 3/4 neutropenia (4%), febrile neutropenia (1%), grade 3/4 thrombocytopenia (13%), grade 3 anemia (1%). One patient developed a bone marrow aplasia. One patient developed a Steven-Johnson syndrome recovered after high supportive treatment. Toxicities caused discontinuation of TMZ in 9 patients (11%). Responses after maintenance treatment were as follows: 7 PR (9%), 6 SD (23%), 4 PD (46%), 7 pts are ongoing. Complete resection and disease stabilization >6 months or response are factors associated with a statistically improvement in 2-yr OS and 2-yr PFS as shown in the Table.

Conclusions. Maintenance treatment with TMZ is safe and effective in pts achieving a clinical benefit from concomitant TMZ + RT.

H11 VEBEP REGIMEN AND HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) IN PATIENTS (PTS) WITH HD AND HIV INFECTION (HD-HIV): FINAL RESULTS OF A PHASE II STUDY OF THE ITALIAN COOPERATIVE GROUP ON AIDS AND TUMOURS (GICAT) STUDY

Spina M.[1], Antinori A.[2], Bibas M.[2], Re A.[3], Mancuso S.[4], Levis A.[5], Talamini R.[1], Tirelli U.[1]

[1]Centro di Riferimento Oncologico, Aviano, Italy; [2]Ospedale L. Spallanzani, Roma, Italy; [3]Spedali Civili, Brescia, Italy; [4]University of Palermo; [5]Ospedale Civile, Alessandria, Italy

Background. The outcome of pts with HD-HIV is still poor, because duration of complete remission (CR) is generally short. To improve the prognosis of HD-HIV, a feasibility study with VEBEP regimen and HAART was started in previously untreated patients.

Methods. CT included epirubicin 30 mg/m^2/day (days 1-3), cyclophosphamide 1000 mg/m^2 (day 1), vinorelbine 25 mg/m^2 (day 1), bleomycin 10 mg/m^2 (day 3) and prednisone 100 mg/m^2/day (days 1-3). HAART was given concomitantly with CT.

Table - H10

		Multivariate (OS)			Multivariate (PFS)		
		HR	95% CI	p value	HR	95% CI	p-value
Subtotal vs total resection	Yes vs no	4.88	2.06-11.53	<0.0001	3.94	1.83-8.48	<0.0001
Response	SD <6 mos vs SD >6 mos vs CR/PR			<0.0001			<0.0001
	SD <6 mos vs response	20.83	7.06-61.44	<0.0001	29.65	10-87.94	<0.0001
	SD >6 mos vs response	1.46	0.70-3.05	0.31	1.48	0.75-2.95	0.26
	SD <6 mos vs SD >6 mos	0.07	0.03-0.18	<0.0001	0.05	0.02-0.13	<0.0001

Results. From September 2001 to December 2008, 73 pts were enrolled. Median age was 41 years. Median CD4+ cell count was 248/mm^3 and 51% of pts had detectable HIV viral load. Stage III-IV was present in 50/71 (70%) patients. Histologic subtypes were: MC 70%, NS 20%, LD 4%, LP 2%, unknown 4%. Four toxic deaths (5%) occurred (septic shock, PCP, hepatic failure and pneumonia during neutropenia). Absolute neutrophil count <500 was noted in 60% of patients. Grade 3-4 anaemia was observed in 38% of pts and severe thrombocytopenia in 22%. Twenty-two per cent of pts had febrile neutropenia with 19 documented infections in 16 pts (4 varicella, 4 bacterial pneumonia, 3 bacterial sepsis, 2 PCP, 1 cerebral toxoplasmosis, 1 esophageal candidiasis, 1 HBV reactivation, 1 HCV reactivation, 1 prostatitis, 1 salmonellosis). CR was obtained in 49/73 pts (67%) and PR in 8/73 (11%). With a median follow-up of 40 months (range 2-106), only 5 of CR pts relapsed. The 3-yr OS and TTF at 24 months were 66% and 63%, respectively. IPS >2 (HR 2.87, 95% CI 1.08-7.63, p = 0.03) and ECOG-PS >1 (HR 2.79, 95% CI 1.21-6.44, p = 0.02) were significantly associated with higher risk of death.

Conclusions. Our data demonstrate that VEBEP regimen combined with HAART is feasible and active in pts with HD-HIV. As observed in HD of general population, IPS is able to stratify patients with different outcome.

This study was supported by ISS grants.

H12 ELECTROCHEMOTHERAPY IN CUTANEOUS MALIGNANCIES: MORE THAN A PALLIATIVE TREATMENT

Benedetto L., Simeone E., Caracò C., Mori S., Marone U., Di Monta G., Aprea P., Maiolino P., Ascierto P.A., Mozzillo N.

Department of Melanoma, soft tissue, sarcoma and head and neck cancers, National Tumor Institute, Naples, Italy

Background. Electrochemotherapy combines electroporation of a tumour with sistemic or local administration of chemotherapy like bleomycin or cisplatin. ESOPE Study (European Standard Operating Procedures on Electrochemotherapy) has demonstrated its anti tumour effectiveness, with 85% of local objective responses on nodules of various malignancies.

Materials and methods. From June 2007 we treated 94 patients (57% with cutaneous/subcutaneous melanoma metastases, 30% with squamous/basal cell carcinoma, 10% with Kaposi sarcoma and 3% with soft tissue sarcoma). We administered intravenously bleomycin at a dose of 15 MUI/m^2, and dose reductions were done in case of renal disfunction based on creatinine clearance. Local or general anaesthesia was decided on the number and location of nodules.

Results. Electrochemotherapy resulted in a safe procedure in all treated patients. In twenty out of fifty-four melanoma patients (37%) with only cutaneous/subcutaneous disease (stage IIIB and IVM1a), it showed a curative role allowing an overall response rate (PR+SD+CR) of 70%, with a long-lasting (more than 6 months) responses in 50% of these patients. In IIIC/IVM1c melanoma patients, electrochemotherapy had a very important palliative role, managing a rapid control of bleeding and also of pain.

Furthermore, similar results were observed for other cutaneous malignancies, with an ORR (PR+CR) of 70% for Kaposi sarcoma and of 60% for basal/squamous cell carcinomas.

Conclusions. Electrochemotherapy can be considered an effective local treatment of cutaneous malignancies. For more difficult diseases like melanoma it can integrate surgery and other systemic treatments (chemotherapy and immunotherapy) without adding toxicity. We are collecting data for better clarifying its systemic effects.

H13 IMMUNOLOGICAL CHARACTERIZATION OF PATIENTS WITH ADVANCED MELANOMA UNDERGONE DENDRITIC CELL VACCINATION

Drago F.[1,2], Granato A.M.[1], Petrini M.[1], Fiammenghi L.[1], Ancarani V.[1], Pancisi E.[1], Malatesta M.[1], Ridolfi L.[1], Nicoletti S.V.L.[1], Riccobon A.[1], Ridolfi R.[1], Guidoboni M.[1]

[1]Immunotherapy Unit, IRST, Meldola (FC), Italy; [2]Medical Oncology Department, AO "Civile Maria Paternò Arezzo", Ragusa (RG) Italy

Dendritic cell (DC)-based vaccines have been increasingly used in cancer therapy and have shown to induce important objective responses in a limited number of patients without any toxicity. However, overall clinical responses rates are still disappointing, and we cannot identify patients who will benefit from DC vaccination. Quali-quantitative characterization of antitumour immune responses, both spontaneous and vaccine-induced, can predict clinical response to immunotherapy. However, the ability of vaccines to induce circulating cancer-specific immune effectors do not always translate into cancer cells killing at all tumour sites. To shed light on this topic, circulating and tumour-associated immune responses were characterized in a series of 32 metastatic melanoma patients who completed at least 5 vaccine courses with autologous mature DC in our institution. To this end, antitumour circulating immune effectors were evaluated by IFN-γ ELISPOT and/or CD107a mobilization assays. Preliminary data showed that our vaccine formulation effectively induces autologous tumour lysate-specific circulating immune responses in the majority of patients. To assess whether the induction of circulating antitumour effector also translates into enhanced immune effector infiltration in tumour sites, we also performed immunohistochemical characterization of tumour infiltrating lymphocytes (TILs) in 26 tumour biopsies taken from 7 patients of the same series, before and at different times after at least 5 courses of vaccine. In most cases, a significant increase of intratumour CD8+ CTLs together with the decrease of FoxP3+ Treg cells was found in postvaccine biopsies. However, in two of these cases circulating immune responses induced by vaccination were not paralleled by concordant change in the amount of tumour-infiltrating CTLs, supporting the possibility that immune escape had occurred in these lesions. Interestingly, in one of these cases the progressive surgical removal of "immunoescaped" tumour lesions led to a NED status that still lasts. These data, besides validating the immunological efficacy of our vaccine, also suggest that extensive immunomonitoring may be relevant for the clinical decision in a multimodal therapeutic approach.

H14 IMMUNOLOGICAL AND BIOLOGICAL CHANGES AND THEIR CORRELATION WITH CLINICAL RESPONSE AND SURVIVAL DURING IPILIMUMAB IN METASTATIC MELANOMA COMPASSIONATE USE PROGRAM

Simeone E., Gentilcore G., Esposito A., Curvietto M., De Rosa P., De Maio E., Caracò C., Sandomenico F., Mozzillo N., Ascierto P.A.

Unit of Medical Oncology and Innovative Therapy and Melanoma Cooperative Group, National Tumor Institute, Naples, Italy

Background. FDA has approved ipilimumab at 3 mg/kg as first- and second-line of therapy in patients with metastatic melanoma. Anyway no clinical parameter has been consistently found to be a surrogate or a predictive marker for response to ipilimumab therapy and only a few immunologic changes (absolute lymphocytes value) have been demonstrated.

Patients and methods. From June 2010 to date we have been treating in the Compassionate Use Program for ipilimumab, at 3 mg/kg, fifty pretreated metastatic melanoma patients. 35/50 patients (70%) completed all four doses and were considered evaluable for clinical response, toxicity and for serum changes of absolute lymphocytes number, LDH and RCP (reactive C protein), and for time to progression (TTP). For RCP evaluation we defined 3 categories: <5 mg/dL for normal values, ≥5 <8 for high values and ≥8 to indicate very high values. We have collected PBMC (peripheral blood mononuclear cells) for T regulatory cells (T Reg) levels and sera for cytokines (IL-10, IL-6 and TGF-β) and auto-Ab (as Anti DS-Dna, Anti-Tg, ANA).

Results. We found in 30/35 (85%) of patients a good correlation between the increase of LDH and CRP and between them and clinical response. We confirmed that the increase of absolute lymphocytes number (ALN) correlates with survival. For patients [17/35 (48%)] with a rapid progressive disease not responsive to ipilimumab, we found that the percentage of Treg increased during the treatment (median 1.8%; range 1%-2.6%); this increase was not influenced by development of autoimmunity. In the responsive patients group [18/35(51%)] the values of Treg remained stable at 0.50% [(10/18 (55%)], while in 8/18(45%) decreased of 0.10% per cycle. At moment, no changes in serum cytokines and antibodies have been found.

Conclusions. ALN, LDH and RCP seem to be predictive parameters of response to ipilimumab. Moreover, very preliminary data show a relationship between the increase of the circulating Treg cell percentage and a bad response to ipilimumab. Further studies are necessary to verify this data.

H15 COMPREHENSIVE GERIATRIC ASSESSMENT-ADAPTED CHEMOTHERAPY IN ELDERLY PATIENTS (> 70 YEARS) WITH DIFFUSE LARGE B-CELL NON-HODGKIN'S LYMPHOMA (DLBCL): FINAL RESULTS AND LONG TERM FOLLOW-UP

Tirelli U.[1], Fratino L.[1], Balzarotti M.[2], Uziel L.[3], Giacalone A.[1], Ferreri A.[4], Santoro A.[2], Spina M.[1]

[1]National Cancer Institute, Aviano, Italy; [2]Humanitas Institute, Rozzano, Italy; [3]San Paolo Hospital, Milano, Italy; [4]San Raffaele Hospital, Milano, Italy

Background. R-CHOP is the standard treatment for elderly patients (pts) with DLBCL. Many pts aged 70 years (yrs) or more are unable to receive R-CHOP and most of them are excluded from clinical trials. Comprehensive geriatric assessment (CGA) is an useful instrument to predict the clinical outcome of elderly pts with cancer. Within the GOL (Gruppo Oncoematologico Linfomi) we started a phase II study to evaluate feasibility and activity of a CGA-driven chemotherapy for these patients.

Material and methods. Patients with no comorbidity received CHOP/R-CHOP; pts with mild cardiopathy received epirubicin instead of doxorubicin; in pts with moderate/severe cardiopathy the use of anthracyclines was omitted; pts with diabetes didn't receive prednisone; in pts with neuropathy vincristine was omitted. Chemotherapy dosage was decided according to CGA: pts with a good score (ADL = 6 and IADL >6) received full doses of CT; pts with an intermediate score (ADL = 5 and IADL >4) received 75%; pts with a poor score (ADL <5 and IADL <5) received 50%.

Results. One hundred pts (41 males and 59 females) have been treated. Median age was 75 yrs and stages III-IV were diagnosed in 51% of pts; 61% of pts received full doses of CT; 25% received 75% and 14% received 50% reduced dose; 86% of pts received an anthracycline and 54% rituximab. Toxicity was quite acceptable. Grade 3-4 neutropenia was observed in 30% of pts, mucositis in 12%, peripheral neuropathy in 9%. Four toxic deaths occurred. Overall, 81% of pts achieved complete remission; with a median follow-up of 50 months, 20% of them have relapsed. The 5 yr-OS, DFS, EFS are 58%, 78% and 50%. It is remarkable that the 5-year specific survival is 72%.

Conclusions. Our results demonstrate that a CGA-driven approach is feasible in elderly pts with DLBCL. This strategy allows to offer a curative approach to all pts with aggressive NHL, avoiding undertreating pts with a potentially cured disease or overtreating pts with severe comorbidities.

H16 IDENTIFICATION OF NOVEL SINGLE NUCLEOTIDE VARIANTS IN GASTROINTESTINAL STROMAL TUMOUR KIT/PDGRFA WILD TYPE (WT-GIST) WITH MASSIVELY PARALLEL SEQUENCING APPROACH

Indio V.[1,2], Pantaleo M.A.[1,3], Astolfi A.[1], Paterini P.[1], Formica S.[1], Casadio R.[2], Martelli P.L.[2], Maleddu A.[3], Nannini M.[3], Pallotti M.[3], Mandrioli A.[3], Lolli C.[3], Saponara M.[3], Di Battista M.[4], Gatto L.[3], Santini D.[5], Catena F.[6], Dei Tos A.P.[7], Biasco G.[1,3]

[1]Interdepartmental Centre for Cancer Research "G. Prodi", [2]Biocomputing Group, Bologna Computational Biology Network, [3]Department of Hematology and Oncological Sciences "L.A. Seragnoli", University of Bologna, Italy; [4]Department of Medical Oncology, Bellaria-Maggiore Hospital, Azienda USL of Bologna, Bologna, Italy; [5]Pathology Unit, [6]Emergency Surgery and Transplant Department, S. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy; [7]Azienda ULSS 9 Treviso, Treviso, Italy

Background. About 10%-15% of adult GISTs do not harbour any KIT/PDGFRA gene mutation and are defined as wild type. Massively parallel sequencing already identified mutations in SDHA gene. The same approach was used to discover other novel putative variants (SNVs).

Methods. Whole transcriptome paired-end RNA sequencing was performed by Illumina GAIIx system using a 75 bases paired-end strategy on tumour samples of two young adults patients (P1 and P2) affected by gastric WT-GIST (age 28 and 30 years). Sequences were aligned with BWA against exon + junction references. SNVmix2 was used for SNP calling, identifying

2045 and 1780 coding non-synonymous novel SNVs in P1 and P2, respectively. After checking misalignments by SAMTools, the variants were filtered to increasing SNPcall confidence: SNVs with quality read score >30 (error probability of 0.1%), total coverage >40, and ratio between coverage of alterate base and total coverage >0.3 were labeled high confidence. Single point mutations were translated at the protein level and their likelihood of being disease-associated was computed with SNP&GO and confirmed with Sanger sequencing.

Results. Private disease-related variants in the two young adult GIST patients were highlighted: in one patient a K1775E substitution in the myosin heavy chain 9 (MYH9) and a R206H substitution in the triosephosphate isomerase 1 (TPI1); in the second patient a V815M mutation in a oxoglutarate dehydrogenase-like protein (OGDHL). MYH9 is involved in cell motility and cytokinesis, while OGDHL is an enzyme of the Krebs cycle, and TPI1 is involved in glycolysis. Interestingly all the mutations that are labeled disease-associated with SNPs&GO are also promoting protein destabilization according to a predictor suited to evaluate protein destabilization upon mutation starting from the protein sequence (I-Mutant3.0). The results are also confirmed with protein structure computational analysis. Sanger sequencing on both tumour and peripheral blood samples found that private mutations were germline heterozygous.

Conclusions. Massively parallel RNA sequencing, followed by data analysis, allows to discover novel single nucleotide variants and to identify new potential target genes in WT-GIST.

H17 BEVACIZUMAB PLUS FOTEMUSTINE IN RECURRENT GLIOBLASTOMA

Lolli I.[1], Dicuonzo F.[2], Silvano G.°, Campanella G.A.[1], Piombino M.[3], Calace A.[a], Cascardi P.[a], Salvati A.[2], Marsella A.R.°, Defilippis V.[1]

[1]Medical Oncology, IRCCS "Saverio de Bellis", Castellana Grotte (Bari); °Radiotherapy, Taranto; [2]Neuroradiology, [a]Neurosurgery, [3]Radiotherapy, University of Bari

Background. Anti-vascular endothelial growth factor (VEGF) therapy is a promising treatment approach for patients with recurrent glioblastoma (GBM), WHO grade IV gliomas.

Bevacizumab (BV), a neutralizing monoclonal antibody to VEFG, has been shown to be effective in this setting, as single agent or in combination with chemotherapy.

In this study, we evaluate the efficacy of BV plus fotemustine (FTM), a third-generation nitrosourea, as salvage therapy in recurrent GBM patients at first relapse.

Methods. Standard therapy with maximal safe surgical resection followed by radiotherapy with concomitant and adjuvant temozolomide had failed in all patients.

BV was administered on days 1 and 15 at 10 mg/kg and FTM on days 1 and 8 at 75 mg/m^2 (induction phase), followed by a 3 weeks rest period.

Control MRI scan with post-Gd T1 weighted and FLAIR sequences was obtained 5 weeks after initiation of treatment.

Maintenance therapy (BV 10 mg/kg and FTM 75 mg/m^2 every 3 weeks) was started in non-progressive patients. Follow-up MRI scan was performed every 3-4 cycles.

The primary endpoint was response and secondary endpoints were progression free-survival (PFS) at 6 mos and 12 mos, median PFS and toxicity.

Results. Eligibility included 15 patients with GBM, at first recurrence after standard therapy, collected from February 2009 to December 2010 (5 females and 10 males with median age of 56 yrs, range 31-70).

The overall response rate (1RC+6RP) was 46.2%; 6/15 pts (39.6%) had stable disease; 2/15 pts (13.2%) had no response. Disease progressed in 11 patients despite an initial response with local (6) or multifocal (2) recurrence or progression of predominantly non-enhancing tumour (3).

The PFS-6 and 12 was 46.2% and 26.4% respectively; median PFS was 28 weeks. The therapy had moderate toxicity with no >grade 3 haematological toxicity (mainly thrombocytopenia) and no CNS haemorrhages. Two patients had thrombotic complications.

Other side effects were fatigue (59.4%), mild hypertension (19.8%) and mild proteinuria (13.2%).

Conclusions. Bevacizumab plus fotemustine is an active regimen associated with acceptable toxicity in recurrent GBM patients.

H18 MULTIMODALITY TREATMENT OF JAW OSTEOSARCOMAS

Codecà C.[1], Ferrari D.[1], Bertuzzi C.[1], Crepaldi F.[1], Broggio F.[1], Violati M.[1], Luciani A.[1], Zonato S.[1], Caldiera S.[1], Moneghini L.[2], Biglioli F.[3], Foa P.[1]

[1]U.O. Oncologia Medica, [2]U.O. Anatomia Patologica, Ospedale San Paolo, Università di Milano; [3]U.O Chirurgia Maxillo-Facciale, Ospedale Galeazzi, Milano

Osteosarcomas (OS) of the jaw are rare mesenchimal tumours frequently diagnosed in the second-fourth decade and account for 6% of all OS. Between 2002 and 2010, 14 patients were treated with a combination of surgery, chemotherapy (CHT) and radiotherapy (RT). Seven pts were female and the median age of the whole group was 36 years. The histologic subtype was osteoblastic in 8 cases (57.1%), chondroblastic in 4 cases (28.6%), both fibroid and mixoid in one case (7.2%).

All patients underwent a combination of chemotherapy and reconstructive surgery. Twelve pts were treated with a regimen of neoadjuvant (NA) polyCHT alternating ifofosfamide, doxorubicin, etoposide and methotrexate. NA polyCT was administered for a median of 3 months (range 1-6) before surgery that proved to be radical in 8/13 pts (61.5%). Surgery was then followed by the same alternating polyCT employed as NA treatment for a median of 3 more months (1-4). In the five pts with marginal involvement, RT (median dose 60 Gy, range 50-66) was added at the end of CHT. The main grade 3-4 toxicities during NA CHT were hematologic and hepatic (67% and 25%), during adjuvant CHT were hematologic, hepatic and neurologic (64%, 21%, 14%) and during RT oropharyngeal mucositis (80%).

The program was completed by all but one patient who progressed after the first cycle of NA CHT. The patient was immediately operated and treated with adjuvant CHT and RT obtaining a complete and currently persistent response. One patient died during adjuvant CHT for a massive hemorrhage in the site of local relapse. Two patients developed metastatic disease during follow-up, the first in the brain and the second in the lung, after 18 and 21 months respectively. At a median follow-up of 48 months the disease-free survival and overall survival were 71.4% and 78.5% respectively.

A complex multimodality approach including CHT, surgery and RT in selected cases can improve the outcome of pts affected by OS of the jaw.

H19 IPILIMUMAB IN PREVIOUSLY TREATED METASTATIC MELANOMA: EXPERIENCE OF THE ISTITUTO NAZIONALE TUMORI OF MILAN

Di Guardo L., Colonna V., Agustoni F., Buzzoni R., Formisano B., Del Vecchio M.

Medical Oncology 2, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy

Background. The incidence of melanoma in the US is increasing faster than any other type of cancer in men and more than any other type of cancer, except lung cancer, in women. For patients with metastatic melanoma, systemic therapies are limited by low response rate, short duration of responses, and 5-year survival rate <10%. Ipilimumab, a novel CTLA-4 inhibitor, is under investigation for the treatment of metastatic melanoma. Results of a randomized phase III clinical trial comparing ipilimumab vs control showed a first-ever OS benefit for patients with previously treated metastatic melanoma. The majority of the reported adverse events consisted in low grade immune-related events involving skin and intestine.

Patients and methods. Since July 2010 we have identified, for ipilimumab-based therapy "as compassionate use", 34 patients affected by previously treated advanced melanoma. Patients characteristics: 16M/18F; median age 52 (range 27-72); ECOG PS 0-1 (100%). In most of the pts the disease stage was M1c (91%) and had received only one previously chemotherapy (59%). According to the phase III trial the induction phase consisted in 3 mg/kg i.v. every 3 wks for 4 administrations. Patients experiencing a documented disease progression after demonstrating a clinical benefit under ipilimumab treatment could receive four more administrations according to the same schedule of the induction phase (re-induction phase).

Results. We observed 6 SD and 1 PR; 11 pts are still on treatment. In 2 pts the treatment was not administered for early rapid disease progression and for the appearance of symptomatic brain metastases. Data regarding PFS, response duration and OS will be showed at the completion of the patients disease re-evaluation.

Conclusions. Our data suggest a certain clinical activity and a significantly good tolerability profile with rash being the main side effect. This expanded access trial is currently ongoing and will go on until the Italian registration of ipilimumab. Shortly we will provide the pending data regarding all the treated patients.

H20 LONG TERM RESULTS OF STANFORD V REGIMEN AND HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) IN 59 PATIENTS WITH HD AND HIV INFECTION (HD-HIV)

Spina M.[1], Gabarre J.[2], Mancuso S.[3], Re A.[4], Schiantarelli C.[5], Talamini R.[1], Vaccher E.[1], Tirelli U.[1]

[1]National Cancer Institute, Aviano, Italy; [2]Pitié Salpetrière Hospital, Paris, France; [3] Centro Aids, Palermo, Italy; [4]Spedali Civili, Brescia, Italy; [5]Niguarda Hospital, Milan, Italy

Background. The introduction of HAART has significantly improved the outcome of pts with HD-HIV. However there are no data on the long term follow-up of HD-HIV pts treated with conventional chemotherapy (CT) regimens. In 2002, we reported the results of a prospective phase II study with the intensive 12-week CT with adjuvant radiotherapy (Stanford V) and concomitant HAART in 59 pts (Spina et al., Blood 2002; 100: 1984-1988).

Methods. To analyze the long term outcome of patients included in the Stanford V and HAART protocol.

Results. The median follow-up is 67months (range 3-156). The 5-yr overall survival (OS), freedom from progression (FFP), disease-free survival and event-free survival are 54%, 52%, 60% and 37%, respectively. The 5-year OS is significantly different in pts with an international prognostic score (IPS) >2 in comparison with that of pts with an IPS ≤3 (84% vs 36%, p = 0.0005). Similarly, the percentages of FFP at 5 years in these groups are 72% and 45% (p = 0.03).

Conclusions. Our data confirm the long term efficacy of Stanford V regimen in combination with HAART in HD-HIV. However, Stanford V is significantly less effective in pts with IPS >2 and therefore new strategies are to be tested in this setting.

Supported by AIRC and ISS grants.

H21 IPILIMUMAB EXPANDED ACCESS PROGRAM (EAP): 50% OF CLINICAL BENEFIT IN 16 EVALUABLE ADVANCED MELANOMA PATIENTS

Nicoletti S.V.L.[1], Guidoboni M.[1], Ridolfi L.[1], Farolfi A.[2], Passardi A.[2], Valmorri L.[3], Ragazzini A.[3], Ridolfi R.[1]

[1]Immunotherapy Unit, [2]Medical Oncology, [3]Biostatistics Unit, IRST Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Meldola, Forlì

Background. Ipilimumab is a fully human monoclonal antibody (IgG1) that blocks CTLA-4 to promote antitumour immunity and has shown to improve overall survival (OS) in patients with metastatic melanoma. Recently, Food and Drug (FDA) Administration has approved its use for advanced melanoma. In Eastern Countries, while waiting for European Medicines Agency's (EMA) approval, clinical trials using ipilimumab or an expanded access program are available. We report the preliminary results obtained using the latter program in our Institute.

Methods. Thirty-five advanced melanoma patients (5 ocular melanomas), 16 males and 19 females, median age 56.5 (range 26-83), entered the study and received at least one administration of ipilimumab 3 mg/kg (given by Bristol Meyers Squibb Italy). All the patients were pretreated, 28 (80%) of them had received more than one line of chemotherapy.

The first disease evaluation with total body CT scan was performed at week 12; progressive disease (PD) had to be confirmed with a second assessment after 4-6 weeks, whereas clinical benefit (CB = responses + stabilisation) after further 12 weeks.

Results. Of 16 (46%) evaluable patients, 3 had partial remission (PR), 1 mixed response (MR), 4 stable disease (SD) and 8 had PD. The overall response (OR) is 25% and CB 50%. At second assessment performed in 8 (23%) patients, 2 were in PR (or in further response, and one in response after PD).

Two (6%) of the 35 patients experienced adverse events (AE) and had to interrupt the treatment prior to week 12. Of the 16 patients evaluated, 3 experienced cutaneous rash G2-G3, 2 diarrhoea G2, 1 hypothyroidism G2, the remaining 10 did not have drug related toxicities.

Conclusions. These data further support the increasing relevance of ipilimumab in the treatment of advanced melanoma even when heavily pretreated. A 50% CB seemingly forecasts even better results if an adequate preselection of patients participating in EAP is performed.

H22 LONG-TERM FOLLOW-UP OF RITUXIMAB AND INFUSIONAL CYCLOPHOSPHAMIDE, DOXORUBICIN, AND ETOPOSIDE (CDE) IN COMBINATION WITH HAART IN HIV-RELATED NON-HODGKIN'S LYMPHOMAS (NHL)

Spina M.[1], Jaeger U.[2], Sparano J.A.[3], Talamini R.[4], Rossi G.[5], Vaccher E.[1], Tirelli U.[1]

[1]Division of Medical Oncology A, National Cancer Institute, Aviano, Italy, for the GICAT; [2]Department of Internal Medicine I, University of Vienna, Austria; [3]Department of Oncology, Montefiore Medical Center, NY, USA; [4]Division of Epidemiology and Biostatistics, National Cancer Institute, Aviano, Italy; [5]Division of Hematology, Spedali Civili, Brescia, Italy

Background. The combination of rituximab plus chemotherapy (CT) is more effective than CT alone in the treatment of high grade NHL.

Objective. To report the long-term follow-up of CDE plus rituximab in HIV-NHL.

Methods. In June 1998, we started a phase II study using infusional CDE (cyclophosphamide 187.5 mg/m^2/day, doxorubicin 12.5 mg/m^2/day and etoposide 60 mg/m^2/day) administered by continuous intravenous infusion for 4 days every 4 weeks and rituximab 375 mg/m^2 i.v. on day 1. HAART was given concomitantly with CT.

Results. Seventy-four patients (pts) have been enrolled. The median CD4+ cell count was 161 (range 3-691) and the median performance status was 1 (range 0-3). Diffuse large B-cell NHL was diagnosed in 72% of pts and Burkitt in 28%. Seventy per cent of pts had advanced stage (III-IV) disease and 57% of pts had an age-adjusted international prognostic index >2. Fifty-two out of 74 pts (70%) achieved a complete remission (CR), 4/74 (5%) had a partial remission and 18 pts progressed. With a median follow-up of 61 months, only 17% of CRs have relapsed and 41/74 pts are alive. The overall survival, disease-free survival and time to treatment failure (TTF) at 5 years were 56%, 81% and 52%, respectively. Four cases of secondary tumours have been observed. No case of late pulmonary or cardiac toxicity has been reported.

Conclusions. The combination of rituximab and CDE in HIV-NHL treated concomitantly with HAART is very active. CR rate (70%) and TTF at 5 years (52%) are comparable to those observed in high grade NHL of the general population. Our data confirm that in HAART era a high proportion of HIV-NHL can be cured.

H23 EPIDEMIOLOGICAL PATTERNS OF ENDEMIC BURKITT'S LYMPHOMA IN NORTHERN TANZANIA

Farolfi A.[1], Masalu N.[2], Musuraca G.[1], Serra P.[1], Ragazzini A.[1], Faustine L.[2], Amadori D.[1], on behalf of Associazione Vittorio Tison

[1]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), Meldola (FC), Italy; [2]Bugando Medical Center, Mwanza, Tanzania

Background. Burkitt's lymphoma (BL) is a highly proliferative B-cell cancer linked to c-MYC translocation. Although it is a rare disease worldwide, in African children is defined as endemic because of its relatively high incidence. In 95% of cases it is associated with EBV and usually presents with facial (mandibular) tumours. Conversely, sporadic BL, rarely associated with EBV, typically presents with abdominal masses. Malaria and HIV infection are other endemic burdens in south-west African children, but a link between these diseases has yet to be confirmed.

Methods. To obtain information on the epidemiology and possible risk factors of endemic BL, we analyzed data from hospital registries of two regions surrounding Lake Victoria in Tanzania: Mara, a rural area in the east and the more urbanized Mwanza in the north-west.

Results. Although malaria was confirmed as endemic in both regions, its incidence in childhood is difficult to determine, whereas HIV incidence was only 3%. Among the 947 cases of BL diagnosed between 2000 and 2009, 493 (52%) were from Mara, and 454 (48%) from Mwanza. The disease occurred more commonly in males (M:F ratio 1.4:1) and at a younger age than females (mean age 6.8 vs 7.6 years; $p < 0.0001$). The majority of females (57%) presented with abdominal disease, with or without mandibular involvement, whereas facial tumours were more frequent in males (51%), a difference that proved statistically significant ($p < 0.0001$).

Conclusions. BL is potentially curable with chemotherapy. In Western countries a strong correlation has been found between BL and HIV infection. However, the low incidence of HIV in our African population indicates that other causal factors may be present, such as malaria or intestinal parasites, which could independently modulate BL risk by influencing immune response to EBV. Interestingly, there seems to be an imbalance in presentation pattern and in age-incidence between males and females. Further collaborative research could help to identify risk factors of BL in African children and to improve currently available treatment.

H24 CONCURRENT CHROMOSOMAL BCL2 AND MYC TRANSLOCATIONS IN LARGE B CELL LYMPHOMA

Pitini V., Arrigo C., Santarpia M., Tomasello C., Marabello G., Sauta M.G., Buemi B., Altavilla G.

Human Pathology Department, Medical Oncology Unit, University of Messina

Background. Concurrent chromosomal BCL2 and MYC translocations involving the BCL2 and MYC protooncogenes in large B cell lymphoma (NHL) (double-hit, DH) recently, have received increased attention (2008 WHO classification, "B cell lymphoma unclassifiable with features intermediate between DLBCL and BL"). Patients with DH lymphomas often present with poor prognostic parameters, including elevated LDH, bone marrow and CNS involvement, and a high IPI score. All studies on larger series of patients suggest a poor prognosis, even if treated with RCHOP or high-intensity treatment modalities.

Aims. We conducted a retrospective study of DLBCL to evaluate the frequency of double-hit B translocations in DLBCL and

to analyse pathologic and/or clinical features correlated with the presence of double-hit translocations.

Methods. DLBCL samples, diagnosed according to the 2008 WHO criteria and derived from 93 patients treated with R-CHOP or HD, have been subjected to FISH using commercial break-apart probes for BCL2 and MYC. Clinical data were collected from patient files.

Results. Double-hit BCL2/MYC translocations were detected in 9 of 93 cases (10%); 7 DLBCL, 1 BCLU, 1 unclassified. All double-hit DLBCL were GCB immunophenotype and showed varying morphology. Ki-67 index ranged from 15-95%. Clinical characteristic parameters included a high IPI score, a high stage extranodal presentation with CNS involvement(4/9). Furthermore DH was associated with an inferior OS.

Conclusions. Our results suggest that DH is more frequent than previously estimated and could not be identified only by morphology or proliferation rate.

H25 SORAFENIB PLUS DAILY LOW DOSE TEMOZOLOMIDE FOR RELAPSED GLIOBLASTOMA, A PHASE II STUDY

Zustovich F.[1], Landi L.[2], Lombardi G.[1], Farina P.[1], Galli L.[2], Porta C.[3], Amoroso D.[4], Fontana A.[5], Andreuccetti M.[5], Galli C.[2], Falcone A.[5], Zagonel V.[1]

[1]Medical Oncology 1, Istituto Oncologico Veneto-IRCCS, Padua, Italy; [2]Medical Oncology, Azienda Ospedaliera di Livorno, Livorno, Italy; [3]Medical Oncology, Policlinico San Matteo-IRCCS, Pavia, Italy; [4]Medical Oncology, Ospedale Unico Versilia, Lido di Camaiore, Italy; [5]Medical Oncology 2, Istituto Toscano Tumori, Pisa, Italy

Background. There are no phase III trials supporting the role of some treatments for relapsed glioblastomas (GBMs). GBMs are very vascularized neoplasms thus antiangiogenic therapies might obtain some antitumoral effects. Recently, an antiangiogenic such as bevacizumab has given prior encouraging results in phase II studies and is under phase III investigation. From phase II studies also low dose protracted temozolomide (LDPT) seems to have some activity at relapse. Basing on these evidences we planned a phase II trial evaluating the activity of a full oral regimen with sorafenib (S), a tyrosine kinase inhibitor with antiangiogenic activity, associated to LDPT in patients (pts) with relapsed GBMs.

Patient and methods. Recruit able pts were enrolled in the study and received S 400 mg bid plus temozolomide (T) 40 mg/m^2 a day continuously till unmanageable toxicity or disease progression. Disease evaluation was performed every 2 months with gadolinium enhanced MRI using RECIST criteria.

Results. From July 2008 to October 2011, 36 patients were enrolled, 18 male, median age was 59.4 (range 36.5-75.6), ECOG PS was 0 in 3 pts, 1 in 20 and 2 in 13. All pts had histological proven GBMs relapsed after surgery, radiotherapy and temozolomide for at least six months. No patient received prior antiangiogenic treatment. Toxicity was manageable; grade 1-2 was (type/pts): hand and foot syndrome (HFS)/7, hypertension/7, diarrhoea/6, anorexia/3, fatigue/9, nausea/4, stomatitis/1, thrombocytopenia/2, toxic hepatitis/3; grade 3-4 was HFS/5, hypertension/1, and thrombocytopenia/2. All pts were valuable for response: 3 pts (8.3%) had PR, 16 (44.4%) had SD and 16 had progression. Median TTP was 2.7 months (CI 95% 1.2-4.2) and median OS was 7.4 months (CI 95% 5.6-9.1).

Conclusions. Based on our experience the combination of S ant LDPT is feasible and safe and has some activity against relapsed GBMs. The TTP of present study is comparable to the one obtained treating a similar subset of patients with bevacizumab (Zustovich et al., Anticancer Res, 12: 5213-6, 2010).

H26 MICRORNAS AS BIOMARKERS PREDICTIVE OF RESPONSE TO DENDRITIC CELL VACCINATION IN METASTATIC MELANOMA

Ridolfi L.[1], Fabbri M.[2, 3], Fanini F.[2], Vannini I.[2], Guidoboni M.[1], Nicoletti S.V.L.[1], Fiammenghi L.[1], Petrini M.[1], Ancarani V.[1], Granato A.M.[1], Pancisi E.[1], Malatesta M.[1], Fernandez-Cymering C.[3], Volinia S.[3], Riccobon A.[1], Croce C.M.[3], Ridolfi R.[1]

[1]Immunotherapy Unit, [2]Gene Therapy Unit, IRST Meldola (FC) Italy; [3]Department of Molecular Virology, Immunology and Medical Genetics, Comprehensive Cancer Center, Ohio State University, Columbus, OH (USA)

Background. Dendritic cell (DC) vaccination has been recently employed for treatment of advanced melanoma patients. Patients underwent effective immunization after vaccine, as shown by positive delayed-type hypersensitivity (DTH) cutaneous test (POS), have longer overall survival, than DTH negative (NEG) patients. Today, we do not have biological markers predicting which patients will develop a positive immunological response, and therefore might benefit from DC vaccination. Differences in DC maturation status are likely crucial to determine the type and strength of induced immunological response. MicroRNAs (miRNAs) are short non-coding RNAs with gene regulatory functions, whose expression is de-regulated in melanoma. We evaluated whether a different expression of miRNAs occurs in immature (iDC) and mature dendritic cells (mDC) of metastatic melanoma patients, and whether this differential expression correlates with the response to treatment, as determined by the DTH status after vaccination.

Methods. iDC and mDC from 10 patients were collected. DC maturation was obtained with a standard cocktail of cytokines (PGE2, IL-6, TNFa, IL-1b). Total RNA was extracted and hybridized with the 4.0 version of the non-coding RNA array developed at the Ohio State University, which determines the expression of 476 different human miRNAs.

Results. Based on our clinical database, univariate analysis to determine whether miRNAs are differentially expressed in POS (n = 4) vs NEG (n = 6) patients, both at the iDC and at the mDC level was performed. A signature of 24 de-regulated miRNAs (10 down- and 14 up-regulated) in iDC of POS patients (better prognosis) vs NEG patients (worse prognosis), and a signature of 31 de-regulated miRNAs (9 down- and 22 up-regulated) in mDC of POS vs NEG patients was identified. Notably, 5 miRNAs (miR-182, miR-150, miR-330-5p, miR-548-3p, miR-556-3p) were common to the two signatures.

Conclusions. This study seems to indicate that DC may present miRNome aberrations potentially responsible for a different response to the treatment and which might ultimately allow the identification of patients who will really benefit from DC vaccination.

H27 AT HOME MANAGEMENT OF APLASTIC PHASE FOLLOWING HIGH-DOSE CHEMOTHERAPY WITH STEM-CELL RESCUE FOR MULTIPLE MYELOMA PATIENTS

Martino M., Messina G., Russo L., Console G., Pellicanò G.*, Di Filippo Scali R.*, Irrera G.

*UOC Ematologia con trapianto e terapia intensiva, *Associazione Italiana contro le Leucemie, Linfomi e Mielosi, Sezione di Reggio Calabria, Azienda Ospedaliera BMM, Reggio Calabria*

Background. After high-dose chemotherapy with autologous peripheral hematopoietic stem cell transplantation (APHSCT) long hospital stays in the aplastic phase are expensive, lead to increased risk of hospital infections and to increasing pressure on available hospital beds.

Aim. To analyze the feasibility of a home care program (HCP) for multiple myeloma (MM) patients receiving high-dose melphalan 200 mg/m^2 (HDM), and undergoing APHSCT to be at home for the aplastic period, without daily hospital visits.

Material and methods. Between July 2010 and March 2011, supportive care in the aplastic phase after APHSCT was transferred from the hospital to the home setting. Eligible subjects included patients with *de novo*, symptomatic, MM treated with a single course of HDM, followed by APHSCT. In case of patient refusal or ineligibility to the HCP treatment, these patients were registered in the inpatient cohort as the control arm. Patients were discharged to their private home the day after stem-cell reinfusion in the absence of contraindications. Hospital transplant nursing staff delivered all supportive care at home and this included blood sampling from the central indwelling intravenous catheter for laboratory investigations and cultures, transfusion of blood products and infusion of parenteral antibiotics. The transplant physician carried out the survey to the home-patient twice a day, with no access to hospital. In case of unexpected problems, patients could consult the transplant physicians 24 hours a day at the transplant center.

Results. Twenty-six consecutive MM patients were treated with HDM and AHSCT. Eight patients agreed to be managed during the aplastic phase at home; 18 patients were not eligible (4 did not have an available caregiver; 4 have not accepted the management at home; 10 patients lived more than 15 kilometers from the hospital). In the 8 transplant cycles in the HCP, patients were discharged on the first day after stem-cell reinfusion in all cases. The patients in the hospital cohort were hospitalized for a median of 18 days. The home care patients spent most of the aplastic period at home, for a median of 12 days, with 4 days in hospital. Readmissions occurred in 2/8 of HCP patients and were because of fever. Febrile neutropenia occurred for a median of 3 and 7 days in the aplastic period for patients in the hospital and home care setting respectively. Other side effects were mild and comparable between the two study groups. No transplant related mortality occurred in both cohorts of patients.

Conclusions. A HCP using HDM is feasible. No unexpected emergencies were encountered, and toxicity did not seem different from the full hospitalization schedule during the aplastic period.

H28 CHOI CRITERIA: A PREDICTOR OF PFS AND OS IN PATIENTS RECEIVING NEOADJUVANT CHEMOTHERAPY FOR SOFT TISSUE SARCOMAS

Porrino P., Boglione A., Bergnolo P., Oliva C., Chiadò Cutin S., Pochettino P., Monasterolo G., Inguì M., Gino G.C., Brach del Prever E., Faletti C., Comandone A.

Ospedale Gradenigo, Torino; Ospedale CTO, Torino

Background. RECIST criteria, based on changes in tumour size, are normally used in the assessment of neoadjuvant chemotherapy (NACT) in soft tissue sarcomas (STS). In the last five years a new kind of evaluation has been introduced: the Choi criteria including volume reduction and tumour mixoid degeneration. In some tumours (GIST, HCC) treated with targeted therapies, Choi criteria seem to better correlate to response and clinical outcomes. This study aimed to determine if in STS undergone NACT, RECIST or Choi criteria better correlate to PFS and OS.

Patients and methods. Thirty-five patients (median age 61 yrs, range 29-78) with locally-advanced not metastatic STS of the extremities received a median of 3 courses of epirubicine and ifosfamide as NACT. CT scans were performed every 3 months. Radiological response to NACT was performed according to both RECIST and Choi criteria.

Results. Following RECIST criteria 8 (22.86%) responders (PR) and 27 (77.14%) stable disease were assessed. On the contrary, according to Choi criteria, 19 (54.29%) responders (volumetric and tumour attenuation) and 16 (54.71%) no change were recognized. The median follow-up time was 50 months (mean 52 months; range 5-97). Following RECIST criteria, in responders group, OS and PFS were 96 months and 86 months. Non responders had 70 months OS and 64 months PFS. Differences were not statistically significant (p .16, p .37). According to Choi criteria, OS and PFS in responders were 96 months and 86 months, in non responders OS was 62 months and PFS was 54 months. Differences were statistically significant (p .02, p .03).

Conclusions. As previously described in GIST, HCC and renal cancer, Choi criteria are better predictive and prognostic factors in patients with STS of the extremities treated with NACT. A wide cooperation with radiologist is requested in order to spread these criteria.

H29 RETROSPECTIVE ANALYSIS OF PATIENTS TREATED WITH SURGERY PLUS CARMUSTINE-WAFERS (CW) PLACEMENT AND SUBSEQUENT FOTEMUSTINE FOR RELAPSED HIGH GRADE MALIGNANT GLIOMAS (HGMG)

Farina P.[1], Zustovich F.[1], Lombardi G.[1], Della Puppa A.[2], Scienza R.[2], D'Avella D.[2], Zagonel V.[1]

[1]Istituto Oncologico Veneto, IRCCS, Medical Oncology 1, Padua, Italy; [2]Azienda Ospedaliera di Padua, Neurosurgery Department, University of Padua, Italy

Background. There is no standard treatment for relapsed HGMG; fotemustine is one of the effective drugs for the second-line therapy with a response up to 30%. The placement of CW (GliadelR) demonstrated effectiveness in patients with HGMG operated at first diagnosis or at relapse. We treated consecutive patients with resected relapsed HGMG with the combination of CW implant and subsequent "adjuvant" fotemustine.

Patients and methods. Consecutive patients with relapsed HGMG suitable for surgery were treated with resection plus CW

implant and subsequent fotemustine at the dose of 75-100 mg/m^2 given weekly for 3 weeks (induction schedule) followed after a rest period of 5 weeks by the same dosage every three weeks. Toxicity was assessed before each fotemustine administration. Disease was evaluated every 3 months with gadolinium enhanced magnetic resonance.

Results. Twelve patients were enrolled, histology was glioblastoma in 10 patients and anaplastic astrocytoma in 2, 6 male, median age 52 (range 29-79), and median ECOG PS was 1. All pts received a prior surgery with radiotherapy and temozolomide administration for 6 or 12 months. Eleven pts were valuable for toxicity that was grade 3 and grade 4 thrombocytopenia (sometimes protracted) in 6 pts and grade 3 neutropenia in 2, 1 patient had an atypical pneumonia. The bone marrow toxicity was mostly during the induction regimen and dose reductions were performed firstly from 100 to 75 mg/m^2 and then omitting the induction schedule, starting with 75 mg/m^2 every three weeks. Eleven patients were valuable for median PFS that was 4.1 months (range 1.4-8.8) with a PFS-6 of 16%.

Conclusions. Sequential implant of CW and fotemustine administration are feasible and safe even if the bone marrow function of these patients may be impaired by prior therapy with temozolomide, especially if given for 12 months, or other agents. In these patients a fotemustine dose reduction is suggested.

H30 GASTROINTESTINAL STROMAL TUMOURS AND OTHER MALIGNANCIES: A RETROSPECTIVE ANALYSIS FROM A SINGLE INSTITUTION

Giuliani J.[1], Marzola M.[1], Indelli M.[1], Aliberti C.[2], Sartori S.[3], Lanza G.[4], Frassoldati A.[1]

[1]Clinical Oncology Unit, S. Anna Hospital, Ferrara (Italy); [2]Unit of Oncological Diagnostic and Interventional Radiology, Delta Hospital, Lagosanto, Ferrara (Italy); [3]Internal Medicine, Section of Interventional Ultrasound, [4]Pathology Unit, S. Anna Hospital, Ferrara (Italy)

Background. The aim of this study is to review clinical and pathological features of GISTs occurring with other malignancies.

Materials and methods. A retrospective analysis has been worked out considering all consecutive patients with GISTs referred to our Institution between 21/02/2002 and 22/06/2010. We analysed the relationship among clinical and biological characteristics of the disease and the occurrence of second cancer.

Results. Twenty-four patients with GIST have been recorded: in 8 cases (33.3%) a second cancer was diagnosed (3 sigmoid adenocarcinoma, 1 rectal adenocarcinoma, 1 prostate adenocarcinoma, 1 breast ductal carcinoma, 1 appendiceal mucocele and 1 gastric GIST), that was synchronous in 6 patients. In the subgroup of synchronous malignancy, GISTs (4 of stomach and 1 of ileum) were discovered during surgery for other gastrointestinal cancers, whereas one case (arising in the duodenum) was diagnosed during the staging procedure for another primary cancer. After a median follow-up of 25 months, 14 patients are alive without evidence of GIST recurrence (58.3%), 1 with a locally advanced disease (4.2%) and 2 with metastases (8.3%); 2 patients (8.3%) deceased for other causes. 5 patients were lost during follow-up (20.9%). In the subgroup of GISTs associated with a second cancer, median age at diagnosis was higher (69 vs 65 years), patients were more frequently male (62.5% vs 43.8%), GISTs were smaller (median size 3 vs 8 cm) and spindle cell histology was less frequent (25% vs 69.2%); all cases were CD117 positive. Other characteristics were similar in the two subgroups, with the exception of risk category, with low or very low cases higher (75% vs 20%), even if not statistically, in subgroup of cases associated with other cancers.

Conclusions. Our series seems to confirm that the association between GISTs and other malignancies is relatively common (10-30%) and would be considered during disease staging or surgery for other gastrointestinal cancer (mainly for gastric sites). Larger studies are necessary.

H31 TREATMENT OF HIGH-GRADE GLIOMAS WITH TEMOZOLOMIDE AND RADIOTHERAPY: ROLE OF O6 METHYL-GUANINE-DNA-METHYL TRANSFERASE (MGMT)

Spinelli G.P.[1,2], Lo Russo G.[1,2], Miscusi M.[1], Calogero A.[1], Rossi L.[1], Papa A.[1], Strudel M.[1], Giordani E.[1], Stati V.[1], Vari S.[1], Basso E.[1], Zoratto F.[1], Tomao S.[1,2]

[1]Department of Medical-Surgical Science and Biotechnology, "Sapienza" University of Rome; [2]Distretto ASL di Aprilia, Oncology Unit, "Sapienza" University of Rome

Introduction. Despite the important progress in the treatment of solid tumours, high grade gliomas (HGGs) remain a poor prognosis neoplasm. We reported the results of the treatment of a newly diagnosed HGGs with standard schedule: radiotherapy (RT) + temozolomide (TMZ) followed by TMZ. Furthermore data were analyzed retrospectively according to MGMT promoter methylation status.

Patients and methods. Between June 2008 and March 2010, 16 newly diagnosed HGG patients with median age of 59.6 years (range 27-80 yrs) were enrolled at Oncology Unit of S. Maria Goretti Hospital in Latina ("Sapienza" University of Rome). All patients received surgical approach but only 5 (31.25%) obtained a total gross resection. After surgery, patients were assigned to receive standard treatment with TMZ (75 mg/m^2) concomitant with RT (60 Gy total dose). After a break of six weeks, patients were reevaluated with magnetic resonance imaging (MRI) and were assigned to receive further 6 cycles of TMZ (150 mg/200 mg/m^2/d x 5dq 28d). MRI and clinical evaluation were performed for all patients at third and sixth cycles. Moreover in all patient MGMT promoter methylation status was retrospectively assessed.

Results. Twelve months overall survival (OS) and progression-free survival (PFS) rates were 62.5% and 43.7% respectively. The data showed a better OS in patients without residual disease than in those no completely resected. In fact only 1of 5 completely resected patients had a relapse within 12 months while all were alive one year after diagnosis. MGMT promoter analysis showed 9 (56.2%) methylated patients and 7 (43.8%) unmethylated. Unmethylated patients had a poor prognosis (OS rate: met = 77.7% vs unmet = 42.8%; PFS rate: met = 55.5% vs unmet = 28.5%). Hematological toxicity (G2-G3) was observed in 42% of patients and fatigue (G2-G3) in 25%.

Conclusions. These mono-institutional results confirm the literature knowledge both in terms of OS and PFS, underlining the prognostic positive impact of MGMT promoter methylation and total gross resection in patients with HGG.

H32 COULD HYPERTENSION BE A POTENTIAL BIOMARKER IN PATIENTS WITH RECURRENT GLIOBLASTOMA TREATED WITH ANTIANGIOGENIC DRUGS? A RETROSPECTIVE ANALYSIS

Lombardi G.[1,2], Zustovich F.[1], Fiduccia P.[1], Farina P.[1], Della Puppa A.[3], Orvieto E.[4], Gardiman M.P.[4], Berti F.[5], Zagonel V.[1]

[1]Medical Oncology 1, Istituto Oncologico Veneto, IRCCS, Padua, Italy; [2]Department of Oncology and Surgical Oncology, University of Padua, Padua, Italy; [3]Neurosurgery Department, Azienda Ospedaliera di Padova, Padua, Italy; [4]Pathology Department, Neurological Sciences, Azienda Ospedale, University of Padua, Padua, Italy; [5]Radiotherapy and Nuclear Medicine Unit, Istituto Oncologico Veneto, IRCCS, Padua, Italy

Background. Numerous antiangiogenic drugs (AD) have been used to treat recurrent glioblastoma (GBM). An important adverse effect of AD is hypertension. The aim of this study was to identify a potential use of blood pressure increase as a biomarker and a predictive factor for response, time to progression and survival from antiangiogenic treatment in patients (pts) with recurrent GBM treated with AD.

Material and methods. Retrospectively, we examined 48 pts with recurrent GBM treated with AD: bevacizumab (21 pts) and sorafenib (27 pts). All patients underwent MRI assessments according to Macdonald criteria every two months or when clinically indicated. Fisher's exact test, univariate and multivariate analyses were performed.

Results. Thirteen (27.1%) and 35 pts (72.9%) performed an AD as third- or second-line chemotherapy, respectively. Median age was 55.1, performance status (PS) was 0 in 8 pts, 1 in 19 pts, 2 in 18 pts and 3 in 3 pts. After two months of treatment 25 pts (52.1%) obtained a disease control (DC): stable disease (22 pts) or partial response (3 pts). The median overall survival (OS) from AD was 6.2 months (CI 95% 4.9-7.6); the median time to progression (TTP) was 2.5 months.

Twenty-one patients (43.8%) developed grade 2-4 hypertension within two months of treatment. No significant association was found between hypertension and response to treatment. According to univariate analysis hypertension was not related to a longer TTP and OS. On multivariate analysis, adjusted for age and AD (avastin vs sorafenib), hypertension was found to be an independent favourable predictor for OS (HR = 0.38, CI 95% 0.16-0.92).

Conclusions. Hypertension may be a valid biomarker in pts with recurrent glioblastoma treated with AD. Thus, patients developing grade 2-4 hypertension within two months of treatment may have a better chance of prolonged OS.

	p	HR	CI 95%
Hypertension	0.032		
Yes (grade 2-4)		0.38	0.16-0.92
No		Ref.	
Age	0.017	1.04	1.008-1.085
Antiangiogenic	0.014	3.5	1.2-1.9
Sorafenib		0.28	0.10-0.77
Bevacizumab		Ref.	

H33 BONE METASTASES FROM GASTROINTESTINAL STROMAL TUMOURS (GISTs)

Nannini M.[1], Pallotti M.[1], Pantaleo M.A.[1,2], Di Scioscio V.[3], Maleddu A.[1], Mandrioli A.[1], Lolli C.[1], Saponara M.[1], Di Battista M.[4], Santini D.[5], Paterini P.[5], Astolfi A.[2], Biasco G.[2]

[1]Department of Hematology and Oncological Sciences "L.A. Seragnoli", [2]Interdepartmental Center for Cancer Research "G. Prodi", University of Bologna, Bologna, Italy; [3]Division of Pneumo-Nefro, Department of Radiology, University Hospital S. Orsola-Malpighi, University of Bologna, Bologna, Italy; [4]Department of Medical Oncology, Bellaria-Maggiore Hospital, Azienda USL of Bologna, Bologna, Italy; [5]Pathology Unit, S. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy

Background. Bone metastases represent a rare event in GIST natural history. Therefore their biological significance and clinical management remain unsettled.

Methods. We reviewed all patients with advanced/metastatic GIST at our institution and focused on cases with bone metastases, describing the clinical and radiological features of these lesions.

Results. Among 71 patients, four had bone metastases. Two were female and two were male, age ranging from 44 to 82 years. All four of them had a high-risk primary GIST, localized in small intestine in three cases, and in the stomach in the other one. Two patients harboured a KIT exon 11 mutations (T >A 69429 (p.V559d) (c.1696_1718del p.N566_P573delinsA), one patient had a WT GIST and in the other one mutational analysis was not assessable. Bone tumour involvement was present at the time of initial diagnosis in two patients, while occurred after 7 and 2 years, during the surveillance program, in the other two. In no one patient bone metastases were the only one site of recurrence, but they were associated to other visceral lesions. Radiologically, the lesions were diagnosed by CT scan. They had a lytic pattern in all cases, with a widespread skeletal involvement. Clinically, bone metastases were symptomatic in three patients, while they were asymptomatic and diagnosed as occasional finding in one patient. Only one case had a pathological fracture. All patients received zoledronic acid in association with TK inhibitors. Two patients had a long stable disease whereas the other two had a quick disease progression. Only one patient was also treated with palliative radiotherapy.

Conclusions. Although bone metastases are an infrequent site of recurrence from GISTs, they may be more prevalent due to the increased patient life expectancy as well as the improvement in imaging techniques. By now their biological background, their prognostic value and their clinical management are unknown. Moreover standard imaging and metabolic criteria for diagnosis and tumour response assessment are still lacking. These data should be collected in large series.

H34 CARBOPLATIN AND DACARBAZINE AS FIRST-LINE CHEMOTHERAPY IN METASTATIC UNRESECTABLE MALIGNANT MELANOMA: RESULTS OF A PHASE II STUDY

Pochettino P., Chiadò Cutin S., Bergnolo P., Dal Canton O., Oliva C., Boglione A., Porrino P., Inguì M., Ottaviani D., Garetto F., Monasterolo G., Comandone A.

U.O.A. Oncologia Medica, Ospedale Gradenigo, Torino

Background. The number of melanoma cases worldwide is increasing faster than any other cancer and remains one of the most treatment-refractory malignancies. Despite decades of clinical trials testing chemotherapy and immunotherapy, a standard first-line treatment for metastatic melanoma has not yet been established, though single agent dacarbazine represents the most common option.

There is increasing evidence that carboplatin is clinically active in the treatment of metastatic melanoma (MM).

Methods. Between January 2007 and April 2011 we conducted a phase II trial in patients with metastatic unresectable melanoma chemotherapy naïve.

The regimen consisted of carboplatin AUC 5 on day 1 + dacarbazine 400 mg/m^2 daily on days 1, 2, 3 every 28 for six cycles.

The primary aims of the study were response rate (RR), time to progression (TTP) and toxicity.

Results. Thirty-four pts were enrolled (22 males, 12 females), 28 pts assessable for RR, TTP and toxicity. Median age was 68 years (range 40-77). Mean number of cycles was 4.6 (range 2-6). Primary tumour sites: 31 skin, 2 choroid, 1 anus.

14% of pts had more than three organ sites involved, 72% of pts had liver metastases, 5% had SNC metastases.

After a median follow-up of 10.8 mo (range 3-24) the RR was 17.8% (2 RC, 3 PR), stable disease in 21.4% (6). Median TTP was 5.2 mo, median OS 10.4 mo. Five pts are still alive (3 of these developed disease progression).

The main side effects were haematological (leuco-thrombocytopaenia G2-3 21.4%, anaemia G2-3 7.1%). No patient discontinued therapy because of toxicity.

Conclusions. Our study confirms that the combination of carboplatin + dacarbazine represents a valid and well tolerated therapeutic option in first-line unresectable metastatic MM. Further evaluation of this regimen, alone or in association with other agents, needs to be considered.

H35 END OF LIFE IN PATIENTS WITH ADVANCED OR METASTATIC SOFT TISSUE AND BONE SARCOMAS: FREQUENCIES AND CAUSES OF SUDDEN DEATH

Oliva C., Garetto F., Monasterolo G., Pittana L.S., Porrino P., Bianco L., Dal Canton O., Chiadò Cutin S., Boglione A., Comandone A.

U.O.A. Oncologia Medica, Ospedale Gradenigo, Torino

Introduction. Soft tissue and bone sarcomas are rare tumours that account for almost 1% of all adult tumours. The annual incidence of STS is 1-3/100,000. Approximately 50%-80% of sarcomas develop local recurrence or metastasis. Metastatic disease can rarely be cured. Causes of death are directly related to site of development and the extension of the disease.

Patients and methods. From 01/2006 to 12/2010, 178 patients, followed by our Institution, died for advanced or metastatic soft tissue and bone sarcomas. Amongst them 31 (17.4%) died for a sudden, unpredictable cause. We defined as "sudden death" an event occurred within 24 hours from the onset of terminal illness and without previous signs or symptoms. We performed a retrospective analysis among patients with previous diagnosis of metastatic soft tissue and bone sarcoma followed by our palliative care unit. Primary objective of the study was to evaluate factors predictable for sudden death.

Results. There were 13 females and 18 males, median age 42 yrs (19-80). Median Karnofsky performance status one month before death was 50. Twenty-three pts were affected by a soft tissue and 8 by a bone sarcoma. Seventeen pts had a limbs neoplasm while in 14 cases the primitive tumour was localized in the trunk. Sites of disease spread were: 15 lung, 9 local recurrence, 6 liver, 2 bone, 2 CNS, 2 lymph nodes. Most frequent symptoms were: pain (64.5%) and dyspnoea (48.4%). Causes of sudden death were: acute haemorrhage (11), pulmonary embolism (8), unknown (5), bowel perforation (4), cerebral haemorrhage (2), spinal cord disruption (1). Fourteen pts died at home while 17 were hospitalized. We found a positive relationship between age younger than 35 years and sudden death (p .05).

Conclusions. A sudden unpredictable death seemed to be a frequent problem in patients with advanced soft tissue and bone sarcomas younger than 35 years. No other patient or disease characteristics were predictable for sudden death risk.

H36 EVALUATION OF THE *IN VITRO* ACTIVITY OF THE $\alpha_v\beta_3$ INTEGRIN ANTAGONIST RGDechiHCIT AGAINST MALIGNANT MELANOMA CELL LINES

Nieddu V., Zaccaro L.°, Sassu I., Cossu S., Del Gatto A.*, De Paola I.*, Galleri G.^, Saviano M.□, Palmieri G., Rozzo C., Pisano M.

*Istituto di Chimica Biomolecolare, CNR, Sassari, Italy; °Istituto di Biostrutture e Bioimmagini, CNR, Napoli, Italy; *Dipartimento di Scienze Biologiche, Università degli Studi di Napoli "Federico II", Italy; □Istituto di Cristallografia, CNR, Bari, Italy; ^Porto Conte Ricerche Srl, Alghero (SS), Italy*

Integrins are a family of eterodimeric transmembrane glycoproteins that plays a key role in tumour growth, metastasis and angiogenesis through signals transduced upon ligation to ECM. In malignant melanoma (MM), one of the most aggressive cancers, changes in integrin expression and intracellular control of integrin function are responsible for the conversion from a stationary to a migratory and invasive phenotype, key step toward the development of this tumour: in particular, an overexpression of $\alpha_v\beta_3$ integrin is linked to a more metastatic phenotype. A new highly selective ligand of $\alpha_v\beta_3$, referred to as RGDechiHcit, containing a cyclic RGD motif with two echistatin moieties, has been demonstrated to have anti-angiogenic properties against endothelial cells in animal models of angiogenesis.

Aim of this study was to evaluate *in vitro* effects of the RGDechiHcit antagonist on MM cell lines. Evaluation of different MM cell lines for cell surface $\alpha_v\beta_3$ specific expression, using flow cytometry analysis, allowed to select 7 MM cell lines with variable expression of $\alpha_v\beta_3$ Cell proliferation, adhesion, and migration were carried out using different concentration of the antagonist RGDechiHcit. With the exception of WM266, proliferation was not significantly inhibited by RGDechiHcit after 24 hours treatment, regardless the $\alpha_v\beta_3$ cell surface expression.

However, striking morphological changes were detected in MM cell lines highly expressing $\alpha_v\beta_3$, indicating a specific role of RGDechiHcit in adhesion and migration. Therefore, adhesion assays were carried out on fibronectin-coated plates for 1 hour using different concentration of RGDechiHcit. In this case, a dose-dependent inhibition effect, which partially correlates with cell surface $\alpha_v\beta_3$ expression, was found. Migration assays through fibronectin-coated transwell membrane were carried out for 6 hours, pretreating cells with different concentration of RGDechiHcit. Again migration inhibition was dose-dependent and seems not to be correlated with the differential expression of $\alpha_v\beta_3$.

Although specificity of $\alpha_v\beta_3$ inhibition by RGDechiHcit is still under investigation, our data demonstrate anti-adhesion and anti-migration, but not anti-proliferative, activity of this compound against MM cells.

H37 RETINOBLASTOMA, THE EXPERIENCE OF BUGANDO MEDICAL CENTER (BMC, MWANZA, TANZANIA)

Masalu N.[1], Ntoinyg V.[1], Spruell T.[1], Collovà E.[2], Puglisi F.[3], Franciosi V.[4], Amadori D.[5], Serra P.[5], Crinò L.[6]

[1]Oncology Department, Bugando Medical Centre-Mwanza, Tanzania; [2]Flow Cytometry and Cell Therapy Unit, Medical Oncology, Fondazione IRCCS San Matteo, Pavia, Italy; [3]Department of Oncology, University Hospital of Udine, Udine, Italy; [4]Medical Oncology Unit, University Hospital of Parma, Parma, Italy; [5]Cancer Institute of Romagna (IRST), Meldola, Italy; [6]Medical Oncology Department, S. Maria della Misericordia Hospital, Perugia, Italy

Background. The incidence of retinoblastoma is estimated to be in about 3 per 1 million children annually, and 40% of cases are hereditary, with bilateral involvement and early age at diagnosis. Retinoblastoma is a malignant neuro-ectodermal tumour composed of small cells and its outcome is related to both stage and time of initial treatment. We present a one year experience of retinoblastoma at the Oncology Department in Mwanza and surrounding area, North East of Tanzania.

Methods and results. At the Oncology Department in Bugando Medical Centre-Mwanza, since January 2009 to December 2010, 1,610 cancer patients were admitted of which 511 were children. Retinoblastoma represents a relevant cause of cancer in this children population with 102 cases, 20% of all the population, second to Burkitt's lymphoma with 358 cases (70%).

Most of the patients presented as advanced stage V-VI disease with massive tumour involving retina or optic nerve and infiltrating orbital with extra sclera extension, beyond the indication of surgical resection.

Because of the absence of radiotherapy unit in the Oncology Department, all the patients have been treated with combination chemotherapy with cyclofosfamide, vincristine, methotrexate.

Conclusions. Retinoblastoma seems to be the second cause of children cancer in Mwanza area in one year of observation, largely exceeding the normal expected incidence in the general population. Delay in diagnosis is the cause of advanced stage presentation in most of the patients, and combination chemotherapy was the optimal available treatment. Retinoblastoma in advanced stages V and VI usually is a chemo-resistant tumour and investigation to define and prevent its important occurrence in Mwanza area is ongoing.

H38 METRONOMIC CHEMOTHERAPY WITH TEMOZOLOMIDE (TMZ), IN COMBINATION WITH CELECOXIB, IN PATIENTS WITH RECURRENT GLIOBLASTOMA: A MONOINSTITUTIONAL EXPERIENCE

Farci D., Ghiani M., Piga A.

Medical Oncology, Ospedale Oncologico A. Businco, Cagliari

Aim. Recurrent glioblastoma is an invariably fatal disease, with the majority of patients progressing within 6 months from the start of treatment. Few treatments are available for this condition, which include angiogenesis inhibitors. We have evaluated in a small series of patients low-dose continuous TMZ in combination with celecoxib, a scheme from which anti-angiogenic and anti-tumour activity is expected.

Patients and methods. Twelve patients with glioblastoma, apparently radically operated and subsequently submitted to "Stupp" (concurrent chemoradiotherapy using TMZ followed by adjuvant chemotherapy with TMZ for 6 cycles), had neoplastic recurrence at brain at MRI, confirmed by spectroscopy. Patients were judged inoperable, and were unsuccessfully treated with second-line chemotherapy (fotemustine or PCV). At further progression we used the following scheme of low-dose continuous (metronomic) TMZ 40 mg/m^2 oral daily in combination with celecoxib 200 mg oral twice daily until progression or toxicity. Patients were M/F: 9/3, age 49-79, all in good general conditions (PS 0-1). Patients were reassessed clinically every month, and with brain MRI after the 3rd and the 6th cycle.

Results. In 10 of the 12 patients there was a response in terms of clinical benefit (2 PR and 8 stable disease), whereas in the other 2 patients there was no response. Median TTP was 4.6 months. Treatment was well tolerated without any notable toxicity.

Conclusions. These results on a limited series of patients suggest that the metronomic schedule of TMZ in combination with celecoxib may represent an active and well tolerated palliative treatment in patients with recurrent glioblastoma, deserving consideration for future prospective trials.

H39 A CASE OF AMELOBLASTOMA OF THE JAW: REPORT OF AN EXTREME CASE IN AFRICA

Di Lascio S.[1], Orlandi A.[1], Iaculli A.[2], Masalu N.[3], Amadori D.[4], Pelo S.[5] on behalf of Associazione Vittorio Tison

[1]UOC Oncologia Medica, Policlinico Gemelli, Roma; [2]UOC Oncologia Medica, Azienda Ospedaliera Bolognini, Seriate (BG); [3]Reparto di Oncologia, Bugando Medical Center, Mwanza, Tanzania; [4]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori di Meldola (Forlì-Cesena); [5]UOC Chirurgia Maxillo-facciale, Policlinico Gemelli, Roma

Background. Ameloblastoma is the most common benign odontogenic tumour, accounting for approximately 1% of tumours and cysts of the jaw and 10% of odontogenic tumours. The tumour is considered very rare in young people, in which it accounts for approximately 10-15% of all reported cases of ameloblastoma. Surgery is often very complex and demolitive, with poor cosmetic and functional outcomes. Here we report the case of a huge ameloblastoma of the jaw in a young african boy, the largest one described to our knowledge.

Case presentation. In May 2010, a thirteen-year-old African patient was admitted at the Medical Oncology Department of Bugando Medical Center (Mwanza, Tanzania) for an enormous, slow-growing jaw mass, increased in volume over a period of about three years and measuring about 16 cm in major diameter. Cytologic analysis performed on a fine needle-aspiration showed an odontogenic tumour. Liver ultrasound and chest X-ray ruled out distant metastases. Patient was then transferred to Italy, at Department of Maxillofacial Surgery of University of the Sacred Heart in Rome and in October 2010 he underwent resection of the mandible with reconstruction with autologous fibula. The final histological examination confirmed an ameloblastoma. The

postoperative course was uneventful, and patient could start eating regularly again after two weeks. He is currently in good conditions, awaiting the implantation of dentures.

Conclusions. We reported the case of the largest ameloblastoma described to our knowledge in literature. Despite the complexity of surgery, reconstruction of the mandible with autologous fibula allowed a very quick restore of the ability to eat, with a marked improvement in speech and other QoL parameters as well. The project has been successfully accomplished through the work of Association Vittorio Tison, which endorsed the creation of a Department of Medical Oncology in Bugando Medical Center actively cooperating with a group of Italian oncologists, since January 2009.

H40 PROLONGED CLINICAL RESPONSE TO TRABECTEDIN AFTER FAILURE OF PRIOR ANTHRACYCLINES AND IFOSFAMIDE IN A 68-YEAR-OLD MAN WITH LUNG METASTASES FROM THIGH LEIOMYOSARCOMA (LMS): A CASE REPORT

D'Amico M., Marino A., Fedele P., Sponziello F., Orlando L., Calvani N., Mazzoni E., Nacci A., Schiavone P., Cinieri S.

Medical Oncology and Breast Unit, "A. Perrino" Hospital, Brindisi, Italy

Introduction. Leiomyosarcomas (LMS) are uncommon tumours of mesenchymal origin, showing smooth muscle differentiation. Prognosis in advanced unresectable LMS is dismal: median survival (MS) is 8-13 months from initiation of first-line chemotherapy and 6 months after failure of standard treatment. Trabectedin is a marine-derived antineoplastic compound, synthetically produced, that has showed anti-tumour activity in pretreated patients (pts).

Case presentation. Mr L.N. was a 64-year-old man when, in September 2006, underwent excision of a 4 centimeter lump in the right thigh and was diagnosed with G 3 leiomyosarcoma, Ki-67 30%, negative margins, pT1a Nx M0 (stage IIA). He initiated follow-up that didn't show any recurrence until September 2008, when a chest computed tomography (CT) scan revealed multiple bilateral lung micronodules. In February 2009 he underwent diagnostic thoracotomy which confirmed the multiple nodules and the biopsy showed metastases from leiomyosarcoma. At that time he was 67-year-old, ECOG PS 0. Between March and July 2009 he received 6 cycles of chemotherapy with epirubicin 90 mg/m^2 d 1, ifosfamide 2000 mg/m^2 d 1-3, mesna 2000 mg/m^2 d 1-3, q 3 wks, developing G 3 neutropenia and having stable disease. In January 2010 a chest CT scan showed progressive disease, so in February 2010 we started trabectedin. He received the first three cycles at the dose of 1.3 mg/m^2 24-hour continuous i.v. infusion, q 3 wks. The chest CT scan after the third cycle showed partial response. He developed G3 neutropenia, G2 thrombocytopenia and G3 transaminases increase, so we continued the treatment at the reduced dose of 1.1 mg/m^2 24-hour continuous i.v. infusion, q 3 wks. Since April 2010 he has been going on trabectedin (16 total cycles) at reduced dosage, tolerating the treatment very well and he has been maintaining the partial response.

Conclusions. Traditionally LMS are considered intermediately chemosensitive. Current chemotherapy options include the use of anthracyclines, ifosfamide, gemcitabine, docetaxel and trabectedin. Trabectedin can provide clinical benefit after failure of conventional treatments.

Session M • Miscellanea

M1 CORRELATION BETWEEN BOTH SERUM OSTEOPONTIN/OSTEONECTIN AND BONE REMODELLING PARAMETERS, INFLAMMATORY/METABOLIC VARIABLES AND SURVIVAL IN METASTATIC CANCER PATIENTS WITH TUMOURS AT DIFFERENT SITES

Astara G., Madeddu C., Demurtas L., Antoni G., Serpe R., Ruggiero V., Mantovani G.

Department of Medical Oncology, University of Cagliari, Cagliari, Italy

Background. Osteopontin (OPN) is a secreted, integrin-binding phosphoprotein that has been correlated with tumour grade and stage and disease progression in several tumour types. Moreover, high OPN levels have been clinically correlated with metastatic bone disease and bone resorption in cancer patients. The secreted protein, acidic and rich in cystein (SPARC) is closely related to progression, invasion, angiogenesis and metastatic process of several malignant tumours.

Aim. The aim of the study was to verify in a population of advanced cancer patients with tumours at different sites whether there is a correlation between circulating levels of OPN and SPARC and clinical parameters (such as bone metastases, pain and quality of life), circulating bone remodeling (skeletal) parameters (alkaline phosphatase, C- and N-terminal fragments of type I collagen, osteocalcin, vitamin D), inflammatory (IL-8 and TNF-alpha) and metabolic parameters (BMI, serum cholesterol and triglycerides). The correlation between OPN and SPARC and survival was also assessed.

Patients and methods. From April 2010 to August 2010, we enrolled 33 metastatic cancer patients with tumours at different sites (M/F: 16/17, mean age 66 years): 17 patients with bone metastases, 16 with metastases not involving bone. OPN and SPARC were measured using an antigen-capture enzyme-linked immunosorbent assay technique. BMI, pain by analogical visual scale and quality of life by EORTC QLQ C30 were assessed. Comparison between groups (controls vs cancer patients and cancer patients with vs without bone metastases) was performed by two-sided Student's t test. Correlation between OPN/SPARC and the other variables was performed by Spearman's correlation analysis.

Results. OPN and SPARC in cancer patients were significantly higher compared to controls but did not differ between patients with or without bone metastases. OPN showed a positive significant correlation with C and N terminal fragments of type I collagen ($r = 0.390$ and $r = 0.410$, $p = 0.024$ for both), IL-8 ($r = 0.390$, $p = 0.034$) and a negative significant correlation with quality of life ($r = -0.400$, $p = 0.025$) and BMI ($r = -0.300$, $p = 0.046$). SPARC showed a positive significant correlation with BMI ($r = 0.360$, $p = 0.049$). Moreover, patients with <3 months survival showed significantly higher levels of OPN in comparison to patients with ≥3 months survival (613.7±229.2 ng/mL versus 195.8 ± 165 ng/mL, $p < 0.001$).

Conclusions. The results of the present study show that high OPN levels are associated with poor survival in advanced cancer patients. Further studies are warranted to assess the role of OPN and SPARC to both monitor the effects of antineoplastic regimens and to assess them as potential targets of new treatment strategies.

This study was partially funded by AIRC (Associazione Italiana Ricerca per il Cancro)-project number 8679.

M2 CASE-CONTROL PHASE II CLINICAL TRIAL TO ASSESS SAFETY, EFFICACY OF THE SAME ANTINEOPLASTIC TREATMENT(S) IN "FIT" ELDERLY PATIENTS COMPARED WITH ADULT PATIENTS WITH CANCER AT DIFFERENT SITES

Massa E., Dessì A., Dessì M., Orgiano L., Tanca F., Mantovani G.

Department of Medical Oncology, University of Cagliari, Italy

Background. We designed a case-control phase II open, prospective non-randomized trial in "fit" elderly (≥65 yrs) cancer patients compared with well-matched adult (45-65 yrs) cancer patients to assess whether the same standard antineoplastic treatment could achieve comparable results as for safety and efficacy. The planned sample size was 125 patients per arm. Endpoints were: safety, QoL, PFS, ORR, dose intensity.

Patients and methods. Only "fit" patients at MGA were included. Inclusion criteria for elderly: histological diagnosis of cancer with either advanced disease with measurable lesions or radically resected (adjuvant); life expectancy >3 mos; adequate baseline functional parameters; written informed consent. Inclusion criteria for adults: the same as for elderly plus ECOG-PS 0-1.

Results. In March 2011, 74 patients were enrolled, 37 elderly and 37 adults, all evaluable for toxicity. Elderly patients clinical characteristics: M/F ratio 19/18; mean age 70.6 ± 4.7 years. Adult patients: M/F ratio, 20/17; mean age 53 ± 5.4. Tumour sites were: colorectal, head and neck, NHL, gastric, uterus, breast, lung, prostate, colangiocarcinoma, pancreas, ovarian; 92.6% of patients were stage IV, 2.7% stage III and 2.7% stage II. In the elderly no grade 4 toxicity was observed whilst non-hematological grade 3 toxicities were observed in 16.21% of patients. In the adult group, grade 4 hematological and non-hematological toxicity was observed in 5.4% of patients; grade 3 hematological toxicity in 35.1% of patients and non-hematological toxicities in 32.4% of patients. The difference was statistically significant ($p = 0.021$) in favour of the elderly. In March 2011, 52 patients were assessable for response: the ORR was 57.7% for elderly and 50.0% for adults. No differences were observed as regards quality of life and dose intensity between the two groups. PFS was 10.0 mos (3-12$^+$ mos) for elderly and 9.01 mos (3-12$^+$) for adults.

Conclusions. At this preliminarly planned interim-analysis, the results seem to suggest that elderly "fit" cancer patients can benefit from antineoplastic treatment both for efficacy and with a safety profile not different from adults.

This study was partially funded by AIRC (Associazione Italiana Ricerca per il Cancro)-project number 8679.

M3 THE "ONCO-AIFA" REIMBURSEMENT FROM "RISK SHARING" RESPECT TO BEVACIZUMAB (BV) IN THE CHEMOTHERAPY (CT) OF METASTATIC COLORECTAL (MCR) AND BREAST (MBC) CANCER PATIENTS

Liguori V.*, Oriolo C.**, Palazzo S.*

**U.O. Oncologia, **Farmacia, Azienda Ospedaliera, Cosenza*

Introduction. We assessed treatment with BV up to progression in patients with response or stabilization after CT with FOLFOX4 + BV in MCR and taxol + BV in MBC, using the "Onco-AIFA" Register for the application and monitoring of the appropriate use of the "risk sharing", which provides a reimbursement of the cost of the drug up to 50% for the first 3 cycles of therapy, a total load of Pharmaceutical Industry from the 15th to the 26th cycle of therapy. We assessed also safety and tolerability of treatment relatively to BV.

Methods. From July 2008 to December 2010 were eligible 55 MCR pts, 41 M (74.5%) and 14 F (25.5%), median age 65 (range 36-81), and 20 MBC pts, median age 58 (range 37-77). The MCR pts received oxaliplatin 85 mg/m^2 IV (day 1) + AF 100 mg/m^2 IV (days 1 and 2) + 5 FU 400 mg/m^2 IV bolus (days 1 and 2), + 5FU 600 mg/m^2 (days 1 and 2) + BV 5 mg/kg (day 3), 1 cycle every 2 weeks, in the event of response or stabilization after 12 cycles, maintenance treatment with BV 5 mg/kg every 2 weeks until disease progression, while MBC pts received taxol 90 mg/m^2 on days 1, 8, 15 every 4 weeks + BV 10 mg/kg on days 1 and 15, in the event of response or stabilization after 6 cycles, maintenance treatment with 10 mg BV/kg every 2 weeks until disease progression. All patients were registered at the AIFA web site for confirmation of eligibility to treatment and the application of "risk sharing".

Results. In the CRC pts, the median number of doses of BV was 15 (range 2-45), 33% discontinued treatment for disease progression, 37.5% discontinued treatment for reasons not dependent on the drug, in the 29.5% the treatment is ongoing. In the MBC pts, the median number of doses of BV was 15 (range 2-38), 50% discontinued treatment for disease progression, 30% discontinued for reasons not dependent on the drug, in the 20% the treatment is ongoing. No patient discontinued for severe toxicity. The majority of adverse events were grade 1/2; 46.8% fatigue; 23.4% hypertensive events (only 4.6% had grade 3 hypertension), 7.8% experienced epistaxis, 1.5% rash. Moreover, the calculation of the reimbursement on the basis of "risk sharing" for patients who have completed the treatment was € 67,298.58 for MCR pts and € 100,710.10 for MBC patients.

Conclusions. The current analysis, confirming that maintenance therapy with BV is well tolerated, showed that the reimbursement from risk-sharing with BV is a complex, time and cost consuming, but useful process; and that the oncologist should pay an ethical attention to recover resources.

M4 SECONDARY NEOPLASM: OUR EXPERIENCE AND PROJECTS FOR THE FUTURE

Rigon E., Negru M.E., Demiri T., Forti L., Saggia C., Bertona E., Sponghini A., Galetto A., Genestroni S., Rondonotti D., Alabiso O.

S.C. Oncologia Medica, AOU Maggiore della Carità, Novara

Introduction. Synchronous and metachronous multiple neoplasm development is a rare event but, lately, it is constantly increasing. Many factors are responsible for the phenomenon: general ageing of the population, genetic predisposition, longer survival of oncological patients, aggressive treatment, combined therapy whose late iatrogenic effects are not completely known.

Materials and methods. In our observation we included patients related to our service for the first time since January 2004 to March 2005.

Results. Out of about 786 patients, we have identified 88 cases (11%) of multiple neoplasms (44 males, 44 females) whose median age was between 70 and 79 years.

Of the 67 patients with known date of diagnosis, 25% were synchronous tumours whereas 75% were metachronous neoplasms. Eighty-one patients (92%) developed two neoplasms, three patients (3%) developed three neoplasms and four patients developed four neoplasms (5%). Even considering the limited sample size, the data showed that head-neck tumours are related to a higher risk of developing second cancers, the seventh decade presented the highest risk of developing second cancers and the risk of developing second cancers was inversely proportional to the time elapsed since the first cancer. In our sample, we have found that 37 patients with breast cancer (42%) developed second cancers at these sites: breast, colon, ovary and uterus. We have identified also the following associations: colon cancer was associated with colon, breast, gastric cancers. Lung cancer was associated with gastric and breast cancers.

Conclusions. The phenomenon of multiple tumours is becoming a serious problem as to require careful monitoring especially in the five years after a tumour. Now we do not know certainly the origin of this problem. Many factors are involved, for example genetic predisposition and environmental exposure. Recent studies and clinical practice have demonstrated a relation between medical treatments and second tumours. A possible hope for the future could be represented by the identification of causes of second neoplasm as to implement appropriate measures.

M5 HIGHLIGHTING SECOND OPINION IN ONCOLOGY: A WIDESPREAD AND PHYSICIAN-NEGLECTED PHENOMENON. RESULTS OF REGIONAL SURVEY

Numico G., Greco M., Galli G., Bocco P., Grasso F., Cucchi M., Malossi A., Alvaro M.R., Trogu A., Spinazzé S., Stella A., Sirotovà Z., Mozzicafreddo A., Cristofano A.

S.C. Oncologia, S.C. Comunicazione, Azienda USL della Valle d'Aosta, Aosta, Italy

Background. Seeking a second opinion (SO) is a normal way of making any important choice in life. When facing with the event of cancer this attitude becomes even more obvious. However, having more than one option does not automatically result in better choices. Moreover, physicians are usually reluctant in favoring this attitude, one of the main reason being that getting a SO is felt as a lack of trust. Research in this field is scarce and consequently knowledge of the phenomenon is limited. Our aim was to gather data directly from cancer patients in various phases of clinical history.

Methods. During a 2-month period we submitted a 13-item questionnaire to every patient accessing to our unit. Family caregivers were invited to join the pt in filling the questionnaire.

Results. Among 220 pts invited to answer the questionnaire 82 (37%) accepted to participate. Mean age was 65, females were 71%; pts with high-level scholarship were 20%; breast cancer 54%; time from diagnosis <1 year 32%, 1-5 years 45%; >5 years

23%. Twenty-three pts (28%) reported having obtained a SO and 7 (8%) reported having obtained two or more SO. The reason of seeking a SO was never a lack of confidence in the treating institution. In the majority of cases was due to a search of a reassuring consult (76%). In 60% the SO was searched through informal ways (usually parental advice) and in 30% through the general practitioner or other physicians. Only in 10% the SO was oriented through a web-based research. In 57% the results of the SO were reported to the treating physician while in 33% were kept confidential. In 76% the SO completely confirmed the suggestion received at the treating institution while in 34% was felt as partially or very different. In 60% the pts reported to be satisfied of the SO, that in 82% was felt reassuring. Only in 18% was reported to be not helpful.

Conclusions. With the known limits of the instrument of the questionnaire, the results suggest that in our region SO is viewed as a normal attitude. It is usually driven through informal ways and often is not reported to the treating physician. Notably, the SO is never linked to a lack of trust. We support that the practice of SO should be further studied, oriented and organized by Medical Societies.

M6 HOW MUCH IS THE LIKELIHOOD OF BEING HELPED OR HARMED (LHH) WHEN ADOPTING TARGETED THERAPY (TT) WITH MONOCLONAL ANTIBODIES (MOAB) IN ADDITION TO STANDARD TREATMENT IN THE TREATMENT OF ADVANCED SOLID TUMOURS (AST)? COMPREHENSIVE ASSESSMENT OF THEIR CLINICAL OVERALL IMPACT ACCORDING TO FDA/EMEA REGULATORY APPROVALS

Bonomi M.[1], Bria E.[1], Pilotto S.[1], Massari F.[1], Sperduti I.[2], Cingarlini S.[1], Auriemma A.[1], Cetto G.[3], Giannarelli D.[2], Tortora G.[1]

[1]U.O.C. Oncologia Medica dU, Azienda Ospedaliera Universitaria Integrata, Verona, Italy; [2]Biostatistics, Regina Elena National Cancer Institute, Roma, Italy; [3]U.O.C. Medicina a Indirizzo Palliativo, Verona, Italy

Background. Number needed to treat (NNT) or to harm (NNH) may be practical tools to quantify the clinical impact of TA for the treatment of AST. LHH, a quality-adjusted ratio between NNT and NNH, represents a patient-centered measure in the context of the evidence-based medicine. With a purely speculative intent for trial design, the aim of this analysis was to have a general overview upon the LHH provided by MoAb in AST.

Methods. Randomized clinical trials (RCTs) providing registration of MoAb by FDA/EMEA were eligible if data for efficacy (PFS, OS), activity (ORR) and safety (grade 3-4 specific toxicities) were available. PFS and OS rates were extracted/derived from curves; absolute differences were determined and NNT or NNH (derived according to the worst drug-specific toxicity) were calculated. LHH was calculated for PFS, and additionally for OS whereas the MoAb was registered for a significant survival advantage.

Results. Fourteen RCTs and settings comparing the MoAb in addition to the standard treatment versus the standard were gathered as listed in the Table. Eight and 6 MoAb were registered for a significant PFS and OS advantage, respectively.

Setting	Specific toxicity	LHH	
		PFS	OS
Bevacizumab (*CRC 2nd*)	Hypertension	5.0	-
Trastuzumab (*MBC HER2+*)	Cardiac	3.3	1.3
Bevacizumab (*15-NSCLC-FDA*)	Hypertension	3.0	1.1
Bevacizumab (*RCC*)	Proteinuria	3.0	-
Cetuximab (*HNSCC*)	Rash	2.7	1.1
Bevacizumab (*7.5 NSCLC-EMA*)	Hypertension	2.7	-
Trastuzumab (*GC HER2+*)	Cardiac	2.6	1.5
Bevacizumab (*CRC IRI 1st*)	Hypertension	2.2	1.2
Bevacizumab (*CRC OXA 1st*)	Deep venous thrombosis	1.6	-
Bevacizumab (*MBC*)	Hypertension	1.4	-
Temsirolimus (*RCC*)	High-glycemia	1.3	1.3
Bevacizumab (*15 NSCLC-EMA*)	Hypertension	0.7	-
Cetuximab (*CRC KRAS WT OXA*)	Rash	0.6	-
Cetuximab (*CRC KRAS WT IRI*)	Rash	0.4	-

FDA/EMEA registered MoAb have a potential average LHH in the range of 1.5-8.0 (these are 1.5-8.0 times more likely to benefit, when balanced with the worst drug-specific toxicity).

Conclusions. In spite of the limitations of a derived-by-curve determination at various time-points weighted with an arbitrary-chosen drug-toxicity, and the non reliable formal comparison between MoAb-LHH based on different drug-toxicities, the benefit provided by MoAb requires to be implemented by the identification of tumour-driven targets, by seeking for sensitivity (or resistance) predictive biomarkers. A cost analysis should be concurrently performed in order to put these data in context with the general health care system.

M7 THE 2011 SURVEY FROM THE GRUPPO ITALIANO DATA MANAGERS (GIDM)

Andreuccetti M.[1], Dall'Agata M.[2], Frati P.[3], Gambetti S.[4], McMahon L.[5], Ragazzini A.[2], Prisco S.[6]

[1]Azienda Ospedaliero-Universitaria Pisana; [2]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) Meldola (FC); [3]Istituto Nazionale Tumori Milano; [4]Azienda Ospedaliero-Universitaria di Ferrara; [5]Azienda ULSS9 Treviso; [6]Fondazione GIMEMA on behalf of the Gruppo Italiano Data Manager (GIDM)

Introduction. For over a decade the GIDM, a non-profit association of Clinical Data Managers (DMs) has been active in representing a meeting point for all study coordinators involved in clinical trials as well as promoting educational courses in clinical research coordination. The present work represents the results of the 2011 survey of Italian Data Managers.

Methods. A survey was mailed to listed Italian DMs to investigate academic background, present working position, remuneration, job analysis and correlated level of satisfaction.

Results. Completed questionnaires were returned from 116 DMs in 15 Regions (Table 1).

DMs are mostly graduate professionals 109 (93%), with PhD qualification (39.6% have completed a Master in Clinical Research), mainly females (87%), mean age 34 yrs (26÷52); 90/116 respondents (77.5%) are employed in Oncology settings, at 50 different Institutions. Contracts and forms of collaboration differ from temporary contracts (co.co.co/co.co.pro), free lance, or scholarships and allowances, amounting respectively to 44.8%,

Table 1

Region	No.	%
Emilia Romagna	30	25.8
Lombardy	21	18.1
Piedmont	12	10.3
Puglia	9	7.7
Campania	8	6.8
Tuscany	7	6.0
Friuli	7	6.0
Veneto	6	5.1
Liguria	4	3.4
Lazio	4	3.4
Sardegna	2	1.7
Umbria	2	1.7
Marche	2	1.7
Sicily	1	0.8
Basilicata	1	0.8

15.5% and 14.7%. Twenty-eight DMs (24.1%) are employed either as hospital administrative staff, or as DMs at private institutions and CROs. Mean monthly gross retribution is reported in the Figure 1, for an average working week of 30-40 hrs (55 interviewees, 47.4%) or over 40 hrs (46, 39.6%). Job satisfaction is highly valued: on a 1-10 scale, 97 DMs (83.6%) rated their score ≥8.

Data for salary satisfaction is less encouraging as 67 responders rated it 4÷7, 19 1÷3, and 26 ≥8.

Conclusions. DM are motivated and skilled professionals with a solid academic background and specific qualification. Unfortunately, not being professionally recognized they have no access to permanent contracts or positions and consequently are confined to temporary, unsatisfying posts.

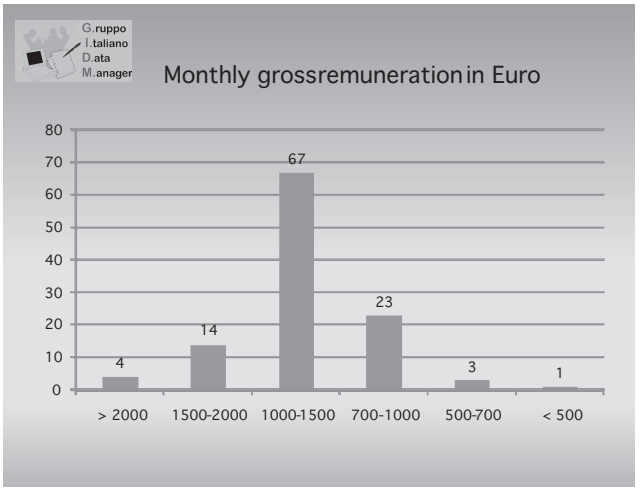


Figure 1

M8 DOES MULTIDIMENSIONAL GERIATRIC ASSESSMENT (MGA) PREDICT ALL-CAUSE SURVIVAL IN A PROSPECTIVE COHORT OF 1038 ELDERLY CANCER PATIENTS?

Basso U.[1], Falci C.[2], Brunello A.[1], Zafferri V.[1], Fiduccia P.[1], Sergi G.[3], Lonardi S.[1], Lamberti E.[1], Castegnaro E.[4], Soldà C.[1], Cossutta F.[1], Chiarion-Sileni V.[2], Monfardini S.[5], Roma A.[1], Borgato L.[1], Zagonel V.[1]

Medical Oncology [1]I and [2]II, Istituto Oncologico Veneto IOV IRCCS, Padova; [3]Geriatric Clinic, University of Padova; [4]Geriatric Clinic, Azienda Ospedaliera, Padova; [5]Istituto Palazzolo, Fondazione Don Gnocchi, Milano, Italy

Background. When approaching cancer in the elderly a key role belongs to predicting tumour-independent life expectancy. Three categories (fit, vulnerable and frail) may be identified using MGA, but we still do not know its actual impact on survival and whether it is independent from tumour characteristics.

Methods. All elderly pts undergoing MGA at our Institution were followed prospectively for survival starting from the day of their first evaluation. Patients were categorised according to MGA subgroup (fit, vulnerable, frail), disease status at the first visit (advanced vs neoadjuvant/adjuvant setting), type of tumour (breast, colorectal, lung, other sites), BMI (<20 VS >20 kg/m^2) and whether or not they received some oncological treatment. Kaplan-Meier survival analysis, logrank test and multivariate Cox regression were applied.

Results. From 09-2003 to 10-2010, 1038 pts were enrolled, median age 77 yrs (range 70-92), 69% female. Main characteristics are outlined in the Table. After a median follow-up of 25 months (1-96), 399 have died (38.4%). Status at MGA predicted all-cause mortality (p <0.001), median survival was reached only for frail pts at 32 months. Significance was maintained in the subgroups with adjuvant/neoadjuvant or advanced disease, treated or untreated pts, breast cancer or "other sites" category, pts with BMI >20, but was lost when only colon, or lung cancer, or pts with BMI <20 were considered. Prognostic role of MGA was found also in the subgroup of 487 breast cancer pts seen in the adjuvant/neoadjuvant setting. At multivariate analysis, fitness maintained a strong impact on survival compared to frailty (HR = 0.45, 95% CI 0.34-0.60) as well as vulnerability vs frailty (HR = 0.69, 95% CI 0.53-0.91).

Conclusions. MGA allows to predict tumour-independent survival probability of elderly cancer patients. The subgroups with colorectal or lung cancer, and patients with BMI <20 were probably too small to reach significance.

Table - All-cause survival probability at 24 months

		Survival at 24 months (univariate logrank test)			
	No. of pts	Fit	Vulnerable	Frail	p-value
Whole cohort	1038	82.4%	70.9%	56.6%	<0.001
Disease status at first visit	1008				
Adjuvant/neoadjuvant	701	92.5%	86%	78.2%	<0.001
Advanced	307	50.7%	35.7%	34%	0.004
Disease site	1038				
Breast	530	95.3%	89.5%	78.8%	<0.001
Colorectal	168	76.1%	62.5%	60.7%	0.231
Lung	85	24.9%	31.3%	18.9%	0.255
Other	255	66.1%	47.9%	39.2%	<0.001
Oncological treatment	1006				
Yes	789	82.1%	70.5%	63.5%	<0.001
None	217	85.4%	79.3%	51.6%	<0.001
BMI	811				
<20 kg/m^2	63	80%	36%	30%	0.322
≥20 kg/m^2	748	95%	75%	63%	<0.001

M9 THE APPROPRIATENESS OF REQUESTS FOR THE MEASUREMENT OF BLOOD TUMOUR MARKERS IN A GENERAL HOSPITAL

Biffi M.[1], Borgonovo K.[2], Petrelli F.[2], Cabiddu M.[2], Cremonesi M.[2], Olejnik K.[2], Barni S.[2]

[1]Clinical Pathology Department, [2]Medical Oncology Division, A.O. Treviglio-Caravaggio, Treviglio, Italy

Background. Blood tumour markers are used by oncologists in cancer patients to discover an early relapse of disease or to monitor response to treatment of patients with evidence of disease. No scientific oncological society suggests their use for screening or diagnosis.

The aim of our study is to examine how appropriate the requests for the measurement of blood tumour markers were in our General Hospital.

Material and method. In 2009 our Clinical Pathology Department received approximately 73,000 requests for the measurement of blood tumour markers, many unnecessary, incurring an expense of more than one million euros. 55% requests came from various hospital wards. We wanted to see if these were strictly necessary according to the diagnosis on discharge of patients.

Results. 20% requests for laboratory tests included the measurement of blood tumour markers. Of the requests coming from within the hospital only 35% were those for oncological patients - according to the diagnosis on discharge. 75% requests were for patients with no clinical history of cancer on admission or discharge.

The majority of requests arriving from the surgical wards included a series of markers - more than 4 in 90% of cases. Even if variable in number, 65% requests coming from the medical wards were for more than 3 tumour markers. In patients with tumours of the colon and rectum, requests in more than 95% of cases were for CEA, CA19.9 and alphafetoprotein. From the surgical wards 40% requests included also CA125, CA 15.3 and PSA.

Conclusions. This study has brought to light the fact that 65% internal requests for blood tumour markers are made for patients wih no medical history of cancer. It has also demonstrated that often these requests are made for groups of markers independently of a suspected disease.

The expense of laboratory tests could possibly be reduced by 50% if unnecessary requests are not made and the money saved could then be used to carry out new diagnostic tests.

M10 TRANSITION TO ELECTRONIC PATIENT RECORD "ONCOSYS" AT THE ISTITUTO ONCOLOGICO VENETO-IOV, IRCCS, PADOVA: THE CRUCIAL ROLE OF A MULTIDISCIPLINARY TEAM

Zagonel V.[1], Basso U.[1], Berti F.[2], Favaretto A.[4], Galtarossa N.[3], Giacomini B.[3], Gomiero F.[5], Paganelli F.[6], Rigato A.[7], Santi J.[7], Villano M.[5], Giacobbo M.[8]

Medical Oncology [1]I and [4]II, [2]Radiotherapy, [3]Nursing Coordinating Unit, [6]Pharmacy, [8]Medical Direction, Istituto Oncologico Veneto IOV IRCCS; [5]Information Technology Department, Azienda Ospedaliera, Padova; [7]*Noemalife Company, Bologna*

Background. Electronic patient records-EPRs offer several advantages over the traditional paper-based charts for organized storage of clinical data of patients, especially in the field of oncology where accurate monitoring of patients' outcome is a crucial step in the evaluation of benefits and toxicities of chemotherapy and targeted agents tested in clinical trials. Moreover, a pooled analysis of costs and appropriateness of treatments is becoming more and more important in order to rationalize resource utilisation throughout the different phases of disease. Oncosys is an EPR distributed by Noemalife and specifically designed for oncology. Oncosys follows the HL-7 semantics for clinical documents exchange and is currently active at the Santa Chiara Hospital in Trento and other Italian Oncological Departments.

Objectives and methods. In November 2009 a multi-step implementation project began at our Institute in order to activate Oncosys at the Departments of Medical Oncology and Radiotherapy. A multidisciplinary team-MT was created by members of each division involved in this complex process: the Medical Direction, the Information Technology Team, Noemalife Company, Medical Oncology I and II, Radiotherapy, Nursing Coordinating Unit and Pharmacy. Activities of this group were prioritised according to the Table below.

Results. Starting from 1st July 2010 each new patient referred to the Medical Oncology Divisions and/or to Radiotherapy generated a single EPR to be shared by all oncologists, radiotherapists, nurses and pharmacists. Prescription and administration of chemotherapy regimens and personalized programs of radiotherapy were efficiently and safely performed by EPR, since no serious clinical event attributable to use of Oncosys occurred. Daily clinical notes were printed, signed and then stored separately in order to keep a hard copy of the EPR to be used in case of peculiar situations (monitoring visits from CRO representatives for clinical trials, internal audits, etc.). Several interventions by members of the MT were required in order to assist doctors and nurses while familiarizing with the system. Continuous feed-back from all personnel was strongly encouraged since the actual experience of Oncosys with real patients generated several queries which were discussed within the MT and often generated requests for technical improvements of the software.

Conclusions. The EPR Oncosys was successfully implemented for new patients in our Institution thanks to accurate planning and continuous monitoring of its use by a MT, therefore switching all previous patients to Oncosys is ongoing. We plan in the near future to develop at IOV the following additional functions in Oncosys: managing appointment lists for visits and chemotherapy administration, one-step printing of administrative forms and requests for new exams, implementation of digital signature in order to avoid printing of daily visits, automatic data exchange with regional and national databases (AIFA).

List of activities of the MT

November 2009-January 2010
- Choice of the system Oncosys, creation of the MT, project plan and prioritization of activities, provisional user's manual.
- Assessment of current workflow for administration of chemotherapy and radiotherapy at IOV in order to make the necessary adaptations to Oncosys.

February 2010-April 2010
- Refinement of EPR records (structure or functions) by continuous interactive feed-back between MT and Noemalife in order to adapt Oncosys to specific requirements of IOV (e.g. clinical notes written by doctors/nurses organized chronologically in a single daily record, allergies highlighted in the main-page….).
- Specific rules for storage of signed print-outs of the EPC (digital signature not available).

May 2010-June 2010
- Teaching activities for all personnel (doctors and nurses) run by MIT members.

- Pilot tests with fictitious patients.

July 2010-December 2010
- Oncosys is used for all new patients, no hand-written clinical notes are accepted for these patients.
- Several interventions by members of MT to help physicians and nurses to familiarize with Oncosys.
- Chemotherapy administration forms produced by Oncosys were frequently checked for errors requiring corrections by the oncologists or the pharmacists. Some observations led to technical improvements of the software and printouts.
- Review of all chemotherapy regimens loaded in Oncosys according to internal guidelines.

January 2011-May 2011
- Implementation of the new 2009 TNM staging system for tumours.
- Image acquisition by scanner in order to store relevant documents (histological reports, external consultations, etc.).
- Identification of sequential steps of daily chemotherapy administration in order to trace time of events in the out-patient clinic (prescription by the oncologist, validation and preparation by pharmacy, start and end of intravenous infusion or oral drug delivery to the patient).
- Elaboration of queries for data extraction and pooled analysis using the software QlikView.

M11 TIME REQUIRED TO START MULTICENTER CLINICAL TRIALS: INDEPENDENT RESEARCH SUPPORTED BY AIFA

De Feo G.[1], Frontini L.[2], Rota S.[2], Pepe A.[3], Signoriello S.[4], Gallo C.[4], Labianca R.[5], Sobrero A.[6], De Placido S.[3], Perrone F.[1]

[1]National Cancer Institute, Napoli; [2]GISCAD Foundation, Parabiago (MI); [3]Federico II University, Napoli; [4]Second University of Napoli; [5]Ospedali Riuniti, Bergamo; [6]San Martino Hospital, Genova

Aim. The aim of this study was to describe the time required for the activation of centers participating in two multicenter nonprofit trials supported by the Italian Medicines Agency (AIFA): FATA, on adjuvant endocrine treatment of breast cancer (Clinicaltrial.gov ID: NCT00541086), and TOSCA, on adjuvant treatment of colorectal cancer (Clinicaltrial.gov ID: NCT00646607).

Methods. Data on activation of the trials were prospectively collected through a web-based system. Three milestones were considered for this study: the date of submission of study documentation to peripheral ethic committees (EC), the date of EC opinion and the date of the signature of administrative agreement. Time is reported in days (d) with median and range values.

Time to EC opinion was calculated as the interval from submission to the date of EC opinion either negative or positive; time to administrative agreement signature (authorization) after a positive EC opinion was calculated as the interval from the date of EC opinion to the date of signature. A submission was considered closed either in case of signature of the administrative agreement or in case of negative EC opinion.

Results. From 01/09/2006 to 13/10/2009 and from 18/05/2005 to 28/04/2009, 105 and 137 centers adhered to the FATA and the TOSCA trial, respectively. Final EC opinion was issued by 97/105 (all positive opinions) and by 137/137 (only 2 negative opinions) centers, respectively, with an overall median time from submission of 105 d (2-887). Contracts were signed with 89/97 and 135/135 centers respectively, with an overall median time from EC opinion of 95 d (1-818). Overall, median time from submission of study documentation to administrative agreement signature was 238 d (15-1065).

Conclusions. Overall, a median time of 8 months was spent to open centers in the FATA and TOSCA trials, approximately 4 months each for EC opinion and administrative signature. The whole process still remains inefficient and far from timelines mandated by law.

M12 TECHNICAL REQUIREMENTS OF ECONOMIC VARIABLES OF ORAL ONCOLOGY DRUGS: AN ANALYSIS CONDUCTED BY THE IRST INTEGRATED DRUGS GROUP (GIFI)

Minguzzi M.[1], Crivelli A.[1], Altini M.[2], Frassineti L.[3], Della Luna C.[1], Di Iorio V.[1], Masini C.[1], Passardi A.[3], Amadori D.[4]

[1]Oncological Pharmacy, [2]Health Care Directorate, [3]Department of Medical Oncology, [4]Scientific Directorate, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), Meldola (FC), Italy

Purpose. Oral oncology drugs are a relatively recent development that have a significant impact on disease management, government resources, patient care and quality of life. In order to optimize the effectiveness and efficiency of their prescription, the following need to be taken into account:

1) *Reclassification:* AIFA Regulation 02/11/10 transferred several oncology drugs, including capecitabine, from the HOSP2 to the A band, opening up the possibility of new and "disturbing" outcomes on patient care and economics. Although most prescriptions are administered in the hospital, this reclassification may have a major financial impact on funds allocation and pharmaceutical care planning; 2) *Care variables:* the decentralization of oral oncology prescriptions requires better coordination of the therapeutic processes, even if information technology can help to solve part of the problem. All oncological pharmacies of the Area Vasta Romagna (5 Local Health Authorities) share a common dispensing procedure using a fully traceable computerized system (developed by Log80-IRST) that connects the paths of drug prescription and administration; and 3) *Cost variables:* many factors are used to assess the cost-effectiveness of intravenous (IV) versus oral medication. These include the direct set-up and administration costs, compliance (given therapy), toxicity, revenues derived or not from drug repayments, and the value of diagnosis-related groups (DRG) and/or social assistance.

Materials and methods. A study was conducted at IRST from June 2010 to March 2011 to assess the cost difference between capecitabine (oral) and 5-fluorouracil (IV) prescription. Actual data from a database of chemotherapy prescriptions was integrated with computerized medical records.

Results and conclusions. There was a significant cost difference between the two drugs tested; nevertheless, the final decision is left to the hospital management. However, one element is clear and unambiguous, the commitment to patient care, monitoring and education, and the compliance optimization of home oral therapy require the same amount of work by the operators as the IV procedure carried out within a health care setting.

M13 DATA MANAGERS WANTED. ANALYSIS OF PUBLIC NOTICE FOR ANNOUNCEMENTS AT ITALIAN PUBLIC HOSPITALS. CONTRACTS, REQUIREMENTS, REMUNERATION, AND CRITICALITIES

Prisco S.[1], Ragazzini A.[2], McMahon L.[3], Gambetti S.[4], Frati P.[5], Dall'Agata M.[2], Andreuccetti M.[6] on behalf of the Gruppo Italiano Data Manager (GIDM)

[1]Fondazione GIMEMA; [2]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), Meldola (FC); [3]Azienda ULSS9 Treviso; [4]Azienda Ospedaliero-Universitaria di Ferrara; [5]Istituto Nazionale Tumori, Milano; [6]Azienda Ospedaliero-Universitaria Pisana

Introduction. No national professional and juridical recognition, nor formal standardized education, or permanent posts are available in Italy for clinical data managers (DMs). Lack of legislation and professional acknowledgement is bypassed by offering a number of temporary positions as scholarships, co-ordinated and continuous collaboration or freelance contracts. An analysis was conducted to evaluate opportunities and profile requirements offered at Italian public hospitals for DMs.

Methods. Web searches were carried out by two independent researchers. Public announcements referring to specific funds (AIFA, AIRC), single projects or protocols and positions at IRCCS and private institutions were excluded from the analysis.

Results. Eighteen announcements from 01/01/2009 to 30/04/2011 were identified. No substantial data was available prior to that date. Full text of 1 announcement was not accessible therefore it was not analysed.

Of the remaining evaluable 17 public notices, 2 referred to 2009, 8 to 2010, 7 to 2011 (Jan-Apr). 94% of positions were offered at Oncology Departments in 9 Regions.

Co-ordinated and continuous collaboration, scholarship and freelance contracts amount to 11 (65%), 4 (23.5%) and 2 (11.5%), at a yearly average gross remuneration of €20,000, €21,000 and €29,000 respectively.

15/17 require a specific degree (Statistics, Biology, Chemistry, Sociology, Pharmaceutical biotechnology, Pharmacy at a minimum). Former experience in data management is a prerequisite in 12 cases, knowledge of English in 6, master and qualifying examination in 4. Only 2 require a high school diploma and previous experience.

Conclusions. Public announcements for DMs increased by 300% in 2010 and a growth of around 150% is expected for the current year. DMs positions are rather temporary and precarious and not recognized by law. Official juridical and professional recognition is warranted throughout the country.

M14 ORGANIZATIONAL ANALYSIS OF THE USE OF ORAL CHEMOTHERAPY: RESULTS OF A SURVEY OF DOCTORS AND NURSES UO ONCOLOGIA OF THE CALABRIA REGION

Iuvaro M.D.[1], Liguori V.[1], Tagliaferri P.[2], Cutuli I.[3], Di Pinto P.[4], Maisano R.[5], Molinaro P.[6], Schito I.[4], Squillace R.[7], Toscano R.[8]

[1]U.O.Oncologia, Cosenza; [2]Università Magna Grecia, Catanzaro; [3]U.O. Oncologia, Siderno; [4]U.O. Oncologia, Castrovillari; [5]U.O. Oncologia, Reggio Calabria; [6]U.O. Oncologia, Lamezia Terme; [7]U.O. Cure Palliative, Catanzaro; [8]U.O. Oncologia, Paola

Introduction. In 2010, medical oncologists and nurses of the Calabria Oncology Department were invited by the steering group AIOM Calabria to participate in an online survey on the use of oral chemotherapy (CT) for cancer patients at their institutions.

Materials and methods. The questionnaire, designed by the Steering Group AIOM Calabria, including 11 questions, was sent via e-mail to 64 oncologists and 128 nurses in Calabria from13 Medical Oncology Services: 3 hospital units, 8 local health service units, 1 university unit, 1 private structure unit.

After 3 e-mail reminders, 24 (37.5%) responses by the physicians and 32 (25%) by the nurses were received.

Results. The informed consent is used in almost all the cases (96%); the physician is directly responsible for the information to the patient on the correct use of the oral CT (agreement in 90% between physicians and nurses); over the 50% of physicians and nurses say that the physician is responsible for information and that he participates in specific training; the use of informative material to the patients is admitted by the 79% of the physicians and by the 47% of the nurses; unanimously the 70% of physicians and nurses say that the prescriptions of oral CT is effected on the models, noting in the 90% of the cases the diagnosis and the dose, and only in 25% the number of cycles and protocol.

Only in 30% exists a clinic dedicate for the oral CT, without some consultation with the chemist (87% of the medical versus the 46% of the nurses), although the communication among the staff physician-nurse-chemist is considered good.

The 30% of physicians and nurses say that is not performed any monitoring on the correct assumption of the oral therapy by the patients.

The 70% of the physicians report to have had adverse events and the 40% serious adverse events from oral CT, but the 50% of the nurses do not know.

Conclusions. Taken account of the affirmation served as V.C. Jordan to St Gallen (16 March 2011) during the Award Lecture "to primary concern must be compliance of the patient with the antihormone treatment regimen. Without treatment compliance, there will be no survival benefit, knows this must be to primary focus for the medical support team", the data of the ns survey on the Calabrian Oncology Department show that the organizational level of the oral therapies in the Region is absolutely insufficient, and that such lack deserves to be recognized as a priority by the regional Sanitary Authorities in the hierarchy of criticality.

M15 DATA MANAGER: FACILITATOR AND COORDINATOR IN CLINICAL TRIALS. THE INTEGRATED EXPERIENCE OF THE TREVISO CA' FONCELLO DISTRICT GENERAL HOSPITAL

McMahon L.[1], Scannapieco G.[1], Rosti G.[2], Ghiotto E.[3]

[1]Dipartimento Innovazione, Sviluppo e Programmazione, [2]U.O.C. Oncologia Medica, [3]Servizio Farmacia Ospedaliera, Ospedale Ca' Foncello, Azienda ULSS 9, Treviso

Accrual to clinical trials (CT) is essential to determine the effectiveness of different approaches and to establish whether beneficial effects are of clinical and statistical significance and therefore new standards of treatment. However, only 2%-5% of eligible patients enter into clinical trials, both for patients' and clinicians' barriers to enrolment.

Among physicians' barriers to include patients in CT is the burden of additional workload and lack of specific staff to manage a number of non-clinical aspects of the trial (for instance preparing EC submission, maintaining regulatory documents, completing and submitting case report forms, involvement in monitoring visits, ensuring compliance with protocols, regulations and Good Clinical Practice). In providing organizational support and quality assurance, data managers' contribution to research may prove crucial to the success of the entire process.

Improved efficiency in clinical trials may also positively impact on the hospital pharmaceutical expenses as innovative drugs/concomitant treatments/extended access programs are made available to patients.

An innovative approach to data management is being carried out at our Regional Hospital, in which an experienced, qualified and certified data manager has been selected by a competitive examination and integrated to cooperate with clinical staff, ethic committee, sponsors and so forth. The data manager is therefore integrated as a part of the institution, not of a single department. Cost for the hospital data manager is practically nonexistent as the whole project is self-founded with no additional costs for the institution. A specific fund has been set up in which a percentage of grants for patients enrolled to For-Profit clinical trials (at P.I.'s discretion), contributions of the requiring units/departments and donations from charities and pharma converge.

M16 ROLi: A NEW APPROACH FOR AN ITALIAN REGIONAL CANCER NETWORK: THE INTEGRATION OF MEDICAL ONCOLOGY, RADIOTHERAPY AND CLINICAL ONCO-HAEMATOLOGY

Caroti C.*, Porcile G.** on behalf of ROLi (Cancer Network of Liguria District), Genoa

**Medical Oncology Department, Galliera Hospital, Genoa; **Agenzia Regionale Sanitaria, Regione Ligura*

Since 2009 the Public and Social Health Plan of Liguria District set up a clinical cancer network comprehensive of all Medical Oncology, Radiotherapy and Clinical Haematology Departments, both of general Hospitals and of Scientific Institutes for Cancer Research. This clinical network included also paediatric onco-haematology. The essential structure of the network is based on the hub&spoke system, where "hub" is represented by a "Cancer Comprehensive Center"-like model, including two cancer scientific institutes (IRCCS) and the more important General Hospital in Genoa. A new regional informatic system for all districts and departments involved will be necessary for communication. The network followed a social and ethical statement including patient-oriented approach, ethical issues and economic sustainability, to assess a global approach to cancer patient care in a true integrated way. Main issues of the project are: clinical governance, health technology assessment (HTA), quality assurance (QA), cost-efficacy and cost-effectiveness evaluation, screening, PDTA (protocol diagnostic therapeutic assistance) and risk management.

In the next three years the main goals will be:

a) patient service, a "care" service as a structure for information, communication, psychological support and assistance of cancer patient during diagnostic, treatment and palliative setting, trying to integrate hospital care (in-patient) with home care and out-patient;
b) clinical trials with "innovative" drugs, especially early phase clinical trials (phase I/II), for enrolment of a greater number of patients in clinical trials to improve clinical results and to try to decrease the costs of medical care;
c) molecular biology tests to enhance the individual patient-oriented clinical classification and therapeutic approach;
d) performance indicators of cancer care process and their monitoring: communication to patients and between operators, quality assurance of diagnostic and therapeutic procedures, clinical audit, clinical results evaluation, customer satisfaction, clinical research development, etc.

First preliminary results will be available in the next months.

Session N • Nursing

N1* ROLE OF LOCAL ASSOCIATIONS IN ENCOURAGING BREAST AND COLORECTAL CANCER SCREENING: THE "DOOR TO DOOR" MODEL

Sanna V.*, Fancellu A.°, Baldino G.*, Cuccu A.*, Contu Marta*, Masala A.*, Alicicco M.G.*, Contu Marianna*, Barbato A.M.*, Contu A.*

**Medical Oncology, Hospital of Sassari, Italy; °Department of Surgery, Institute of Clinica Chirurgica, University of Sassari*

Widespread use of screening has resulted in a significant reduction in cancer mortality. Health care providers suggest one or more tests for cancer screening, including faecal occult blood test (FOBT) and standard colonoscopy in people aged 50 or more for colorectal cancer and mammography in women aged 50-69 for breast cancer. Adhesion to screening programs is low accounting for only 48-66% of the target population. The existence of socio-territorial organizations could be a helpful tool for improving health governance. The objective of this study was to verify whether screening participation rates for breast and colorectal cancer can be increased by involvement of local associations (Preventive Services Task Force, PSTF).

In our pivotal project, the PSTF were both the Association of Onco-hematology "M.A. Pinna" that is connected with the institution ASL n°1 of Sassari and a local association named "Non solo Cioga". The latter is located in Sedini, a little town in the land of Sassari with 1,461 inhabitants.

We established a multistep program:

- identification of existing socio-territorial organizations;
- development of objectives and priorities: optimal information ("door to door") and equal access to screening service; the "door to door" model consisted in detailed information, given by the PSTF, about the advantages of screening programs;
- connection with an institution able to manage the whole screening process: the ASL n. 1 of Sassari.

In Sedini, 168 on 202 people (80%) were submitted to mammographic screening and 329 on 395 people (80%) underwent FOBT. FOBT was positive in 6% (20/329) of population; among them, compliance in colonoscopy screening was 93% (16/20). In detail, 25% of them had inflammation and/or haemorrhoids, 13% hyperplasia, 50% adenomas, 6% *in situ* carcinoma, and 6% invasive carcinoma.

We highlighted that PSTF involvement may enhance participation in colo-rectal and breast cancer screening. Furthermore, PSTF has an important role in improving the ability of local government in public health.

N2* NUTRITION IN CANCER PATIENTS: A MULTIDISCIPLINARY TEAM FOR A PROSPECTIVE STUDY

Terpin R.[1], Agostini S.[2], Calligaris M.[3], Di Camillo E.[1], Foghin L.[1], Gon S.[1], Miceli B.[1], Fontana R.[1], Perlazzi R.[1], Russo F.[1], Stacul A.[1], Zandigiacomo L.[1], de Pangher Manzini V.[1]

ASS 2 "Isontina", [1]SOC di Oncologia, [2]Servizio di Dietetica, [3]Distretto Basso Isontino

Background. For many reasons (especially when the site of cancer is in head and neck and gastro-intestinal tract, or adverse effect of chemo and radiotherapy, psychological distress) the nutritional status in cancer patients can be deteriorated. It is well known that well-fed patients feel better and also tolerate better the antineoplastic treatments. Therefore, it appears useful, using a simple and validated method, to perform a nutritional evaluation in cancer patients to offer them, if necessary, nutritional and psychological support. The aim of the present study is to evaluate the nutritional risk in all new patients seen at the Struttura Complessa di Oncologia of the ASS n. 2 "Isontina".

Methods. The team dedicated to this study is composed by nurses, an oncologist, an internist, a dietician and a psychologist. At the time of the first oncology evaluation all patients are submitted to the nutritional screening using the MUST test, where point 0 requires monitoring and participating in the information groups if in chemotherapy, point 1 monitoring and participating in the information groups even if out of chemotherapy, and point 2 activation of the nutritional support. Data derived from MUST are enclosed in the personal oncology record of the patient and also recorded in a data base together with psycho-social information and data regarding staging of cancer and type of treatment. Repetition of the Must test is foreseen at 2 or 3 months intervals. Subsequently, according to the first MUST results, the patient is directed to the simple nutritional follow-up or to an individual nutritional support/therapy. Moreover, all patients treated with chemotherapy are invited to participate in the information groups (dedicated to patients and their relatives), that is, two meeting groups at three weeks intervals. In the meeting both the dietician and the psychologist give general information about the role of nutrition, nutrition in the normal setting and in the illness setting, the role of an adequate nutrition to preserve a correct nutritional state, and the nutritional problems related to the illness. A long discussion time is reserved in each meeting and some illustrative depliants are delivered. Finally, patients in stage 2 MUST (those at just deteriorated nutritional state or at serious nutritional risk) are submitted to the nutritional team dedicated to artificial nutrition.

Results. From October 2010 to March 2011, 133 patients (98% of the admissions in Oncology) have been submitted to the first MUST, 58 to the second. The series is composed by 83 women (mean age 68 years, range 25-87) and 50 men (64, 43-91). The most frequent types of cancer have been breast (42 cases), colon (17), lung (10), prostate (8), kidney (59) and ovary (5) cancer. Fifty-seven patients have been treated with chemotherapy, 34 with hormonotherapy, 9 with targeted therapy, 31 with radiotherapy, 36 were submitted to the follow-up only. Results of first MUST (122 cases valuable) are as follow: point 0 in 101 patients (83%), 1 in 9 (7%) and 2 in 12 (10%). Results of the second MUST, performed in 58 cases at a mean interval of 2 months, are: point 0 in 51 patients (88%), 1 in 3 (5%), 2 in 4 (7%). Twelve patients, according to the flow chart, have been submitted to the nutritional team dedicated to artificial nutrition. In the same period 3 meetings, each consisting of two sessions, were performed with a mean participation of 6 people to each meeting and with a high degree of satisfaction.

Discussion. Nutritional evaluation in cancer patients is feasible and easy to perform with a multidisciplinary team composed by the different sanitary personnel involved in the topic. In a prospective unselected series seen at a general hospital, like the one presented in this study, a deteriorated nutritional status requiring a nutritional support is present, at the time of the admission in Oncology, in 10% of the cases. Highly appreciated appear the information about a correct nutrition delivered during the meetings.

N3* ORAL CHEMOTHERAPY MEDICATIONS: NURSE INTERVENTIONS TO INCREASE ADHERENCE AND KEEP PATIENTS SAFE

Oliboni M., Ciccarelli L., Alestra S., Orlando B., Mariotto M., Terzi A., Coati F., Lunardi G., Nicodemo M., Venturini M.

Ospedale Sacro Cuore Don Calabria, Negrar (VR)

Background. Much more patients are receiving oral chemotherapy. Domiciliary treatment needs a tight control by oncologists to obtain good adherence to treatment and keep patients safe. Aim of this study is to explore the feasibility of a nursing intervention in empowerment and monitoring of patients who are taking oral chemotherapy.

Methods. We organized a routine practice, like for intravenous chemotherapy, managed by oncology nurses familiar with oral CT drugs. Patients, who had to assume oral drugs, after the briefing with the physician, received by nurses all necessary information about drug intake, safety and storage, side effects, symptom management, contacts for any problem. Nurses ensured that patients understood both the goals of treatment and the risks associated. With drug delivery, patients received a diary (detailed for each treatment) reporting all instructions given by nurses. On the diary patients could also register daily drug intake (pill count) and list their side effects (graduated by a 4-degree subjective scale). Patients had to return the diary at the end of each CT cycle.

Nurses contacted patients by phone during the first two cycles of chemotherapy to assess patient adherence to treatment and their side effects. We set two questionnaires to evaluate patient's education to oral medications before and after nurse intervention and one to assess patient's satisfaction.

Results. Sixty-eight (93%) out of 73 diaries given were returned from patients most of them (>90%) completely compiled in dosage and side effects. Empowerment of patients was useful especially in behaviours to have in the case of drug intake oversight or side effects onset. Phone calls were generally well accepted by patients and were a valid means for side effects management. Satisfaction for all nurse interventions was very high in all patients.

Conclusions. Patient empowerment by nurse, the diary detailed for each oral medication, phone-based nurse surveillance may be useful to prevent the occurrence of severe toxicities, improving compliance to oral chemotherapy medications.

N4* ONCOLOGY NURSING IN EARLY DETECTION OF ADVERSE EVENTS FROM MAINTENANCE BEVACIZUMAB IN METASTATIC COLORECTAL CANCER

Crocetti C., Scarlata D., Lucerna G., Petruzzella N., Putino A.M., Arnaud M.T., Garbiglia P., Nante M., Demichelis M.M., Fora G., Spadi R., Ciuffreda L., Racca P.

ColoRectal Cancer Unit, Medical Oncology 1, Hematology and Oncology Department, A.O.U. San Giovanni Battista, Turin

Background. The use of bevacizumab is increasing both in combination with chemotherapy and alone in maintenance therapy for metastatic colorectal cancer (mCRC). Specific side effects of this drug are hypertension, proteinuria, bleeding events, thromboembolic events and wound-healing complications. Oncology nurses play a key role in early recognition of adverse events and in patient education, facilitating the optimal use of bevacizumab especially when it is administered alone without chemotherapy for maintenance schedules.

We would like to evaluate through a specific questionnaire that a good and specific nursing team can recognize early the most common side effects of the infusion of bevacizumab at 7.5 mg/kg and improve the Quality of Life (QoL) of the patients in terms of less medical consultation, less time spent in day hospital (DH) and better caring.

Methods. All patients were screened by nurses using a checklist made of questions covering the main side effects of bevacizumab. Patients not reporting any of these side effects were directly managed by the nursing team while the others were referred to medical consultation.

Results. From February 2009 to April 2011, 20 patients (11 males) underwent maintenance therapy with bevacizumab for a total of 180 accesses to our DH. Only 43 times a medical consultation was required: 14 and 2 patients had respectively hypertension more or equal than 150/90 mmHg before and after the infusion; 3 patients reported chest pain, 9 dyspnea, 1 hypertermia, 9 bleeding and 4 had dipstick-proteinuria G2. All screened patients reported satisfaction at the reduction of the time spent in DH due to the new management of bevacizumab infusion.

Conclusions. Only 23% of patients that accessed the DH to receive maintenance bevacizumab needed a medical consultation thus improving the quality of care perceived by patients due to the reduction of time spent in hospital and with the additional benefit of easing clinician's practice.

N5* THE SAFETY AND DIGNITY OF OLDER PATIENTS AND NURSES DURING PATIENT HANDLING

Leo S., Bellante T., Dell'Atti A., Spedicato P., Visconti A., Gambino A., Petrucelli L., Saracino V., Accettura C., Gnoni A., Lorusso V.

Ospedale Vito Fazzi, Lecce, Italy

Background. During cancer disease, some patients show difficulties to move themselves and sometimes, when they are hospitalized, they need nurses help to approach to handling. This could be caused by: advanced age, disease stage, comorbidities, presence of bone metastases, chemotherapy or radiotherapy side effects, other problems, such as pain, fever, asthenia, anorexia.

Methods. In the period 15/Dec/2010-15/Mar/2011, 20 elderly patients with advanced cancer, median age 74.5 years, hospitalized for more than 3 days and unable to move themselves, were interviewed using a 16 items questionnaire to explore patient's emotions during the handling.

Results. All patients interviewed need for help by nurses to move themselves and most of them (95%) don't feel ashamed to ask help. When nurses help to move, most of patients (90%) feel security, relief, quiet, confidence, instead only 5% feel anxiety and only 5% feel shame and mortification. Patients want from nurses: kindness and ability (45%), patience and encouragement (40%), respect, care and assistance (60%). Only few patients (20%) wave to call nurses to receive help to move themselves, due to shame (25%), patients would be able to move oneselves (75%), patients don't accept to depend on other people (75%).

Conclusions. Patients don't judge handling technique, but they express some needs: to be identified like a single and specific person, to be treated with kindness, to receive respect of their dignity and pain, to cooperate relating their limited capacities, to have encouragement to relieve their depression and shame for their health status. Every patient needs a different approach for handling, relating to culture, grade of handicap and disease stage. To obtain this, it is necessary to have an empathic attitude towards all patients: nurses, and in general all medical staff too, should be able to give care and attention as much as possible to ill people.

N6* "SOS-SPIRITUAL ONCOLOGICAL SURVEY": THE RECOGNITION OF A NEED FOR THE PLANNING OF ASSISTANCE

Ricciotti M.A., Cristina G., Gareri R., Capomolla E., Felicetti V., Cifaldi L.

U.O.C. Oncologia Medica, Azienda USL RM G, Ospedale Parodi Delfino Colleferro, Rome, Italy

Introduction. Spirituality is a human experience aspect which changes over a person's lifetime and may be affected by illness. Although only few Italian studies are available, literature evidence about a relationship between spirituality and medicine is increasing. Spirituality is an aspect difficult to measure, little expressed by patients and little noted by physicians.

Aim. In order to assess spiritual needs and resources in a clinical setting of cancer patients (CP) the "SOS-Spiritual Oncological Survey" questionnaire was developed.

Patients and methods. Since 1st April 2011 SOS questionnaire was administered to 80 CPs, with an ad hoc 10 items inquiring about spirituality, cancer disease, community relationship, coping with the disease, role of health care in relation to this issue. One item was qualitative-descriptive, quantitative responses (9 items) were coded according to a 4-point score: 1 = not at all; 2 = a little; 3 = considerably; 4 = very much. CP showing evidence of psychiatric disease or cognitive impairment was excluded.

Results. Eighty CPs filled in SOS showing interest for the test (20 males, 60 females; age 66 ± 11 years; 27 gastro-intestinal, 25 breast, 6 lung, 13 genito-urinary, 9 other cancer; 1 not believer, 78 Catholics, 1 Jehovah's Witness). For 72 CPs it was simple to fill in SOS and for 8 CPs it was a little difficult. The educational level did not interfere with the filling in SOS. Spiritual life of 57 CPs changed during the course of the disease, increasing in 45 CPs and decreasing in 12 CPs. Sixty-seven CPs felt that health care should also be concerned with this aspect to improve the quality of care.

Discussion. Our preliminary data suggest that proper identification of spiritual needs and resources may improve CP's knowledge first and then the quality of care. Ultimately, it will lead to a better integration between the network of formal and informal care support. SOS can be a helpful starting point to evaluate the importance of CPs beliefs, and their intersection with health care.

N7 ACTIVE PHARMACOVIGILANCE PROJECT: A REAL NEED FOR THE ONCOLOGIST

Barni S.[1], Rivolta A.L.[2], Ronzoni M.[3], Rossi F.G.[4], Galfrascoli E.[5], Fasola C.[6], Panzarino C.[7], Lovino G.[8], Comandè M.[9], Pozzi E.[10], Rizzi A.[11], Guarneri P.[1], Farina G.[5]

Medical Oncology, [1]Treviglio BG; [3]S. Raffaele MI; [4]INT MI; [5]FBF MI; [6]Sacco MI; [7]Desio MB; [8]S. Matteo PV; [9]Melegnano MI; [10]Maugeri PV; [11]Poliambulanza BS; [2]Farmacovigilanza Regione Lombardia

Background. In Italy the culture of reporting adverse events (AEs) appears inadeguate. Medical oncologists do not consider adverse reactions to treatment as seriously as other specialists; severe toxicity is often considered acceptable, evaluating it to be "routine" or expected event. As more drugs are becoming available in Medical Oncology, often with poorly defined toxicities and low risk-benefit ratio, the Region of Lombardy has introduced a specific pharmacovigilance plan.

Patients and method. Ten oncology departments in Lombardy were involved in this project. An electronic card for collecting reports of AEs considered as severe (life-threatening or leading to permanent disability or death), or less severe (grade 3-4 toxicity requiring hospitalization, unexpected and with unknown effects) has been introduced. From March 2009 to October 2010, 605 AEs were reported: 434 (72%) were defined as not being serious and 171 (28%) severe.

Results. 40% AEs reported consisted of skin and subcutaneous tissue damage, systemic disease or site of drug administration (33%), gastrointestinal disorders (30%), respiratory or mediastinal disease (25%) and lymphatic system disorders (19%). The outcome of AEs was also assessed. Complete resolution was obtained in 343 cases (57%), improvement in 171 (28%), no change or worsening in 33 (5%), resolution with sequelae in 18 (3%) and death in 12 cases (2%). The onset of AEs led to suspension of the drug in 60% patients. Pharmacological intervention was required in 59% cases and dose modification of anticancer drugs was needed in 11%. Drugs causing AEs more frequently were: oxaliplatin (14.3%), docetaxel (12.4%), 5-fluorouracil (9.2%), paclitaxel (9%) and rituximab (8.4%).

Conclusions. This ongoing study has increased the attention of oncologists to pharmacovigilance, leading to a significant increase in reports of AEs. An evaluation related to different drug toxicity (brand vs generic) is in progress.

N8 COMMUNICATION BETWEEN MEDICAL CORPS AND TERMINAL ONCOLOGIC PATIENTS

Crudeli R., Corsi C., Ferrarini A., Lorenzani D., Marchetti A., Ruffini L., Zanetti L., Orlandi M., Tartarini R., Simonini M., Cantore M.

Oncological Department, Carrara city Hospital, Azienda USL n.1 Massa e Carrara, Italy

A study has been made in the Oncology Department of AUSL1 Massa-Carrara to evaluate how communication between doctor, nurses and patients changes during terminal pathology.

Thirty-five medical operators of the 4 day hospitals and of the recovery wards have participated in the study, 10 doctors, 25 nurses of which 6 men and 29 women.

One questionnaire has been administrated twice: the first time referring to the patients at the beginning of pathology and the second one regarding patients with terminal pathology.

The "Health care communication questionnaire counseling" was used (Gremigni and Sommaruga, University of Bologna).

The questionnaire measured four items:

- capacity of patients problems solving;
- respect towards patients;
- hospitality towards patients;
- non verbal communication.

The operators have esteemed themselves and feel competent to face the relationship with patients whether at the beginning of the illness or at the terminal part of the same illness.

The health operators don't attribute their stress to relationship with patients.

Regarding the different gender, females feel more competent in the non verbal communication while males feel more competent in resolving practical problems.

The present study gives subjective information about communicative modality of health operators with patients using a self evaluation, a new system that can be used as a starting point to individualize areas where communication can be improved.

Attention must always be placed on the patients, keeping in mind his or her decision making ability.

N9 "YOUR NOTE-BOOK" WORDS AS A PART OF THE CURE IN CANCER PATIENTS

Fontana R., Di Camillo E., Foghin L., Gon S., Miceli B., Perlazzi R., Russo F., Stacul A., Terpin R., Zandigiacomo L., de Pangher Manzini V.

ASS n. 2 "Isontina", Ospedale di Gorizia, SOC di Oncologia

Background. The cure of cancer patients includes several aspects, such as anticancer treatment, palliative therapy, and psychological assessment and support. In other words, cancer patients need not a simple cure, but rather a global care. For the sake of a better care it appears very important to create in the Oncology Units a quiet environment aimed at encouraging empathic relationships between patients and sanitary team. In this setting talk retains a very important role. Every day, during therapy sessions, clinical controls, even in waiting rooms, patients tell about their fears, hopes, doubts, plans. Talks regard not only the illness but also the past, present and future of everyday life. Sanitary personnel listen, answer, encourage, and in their turn talk about professional and daily subjects. So, a close relationship between patients and the oncology team (nurse and oncologist) can be brought on. For this reason it can be stated that "words are an important part of the cure". However, words can be exchanged both orally and in writing. Writing allows time and requires time and attention, therefore written words, although they lose immediacy, gain in depth of feeling. The aim of the present study is to provide the patients of the Struttura Operativa Complessa di Oncologia of ASS "Isontina" with a tool to record their written words.

Methods. A ring folder, very similar to the folder used for collecting clinical data of the patients, has been defined "your note-book" and offered to everyone who wished to record ideas, wishes, suggestions, criticism, thanks, proposals for amelioration, and overall anything the patients would like to say to the oncology team or for itself. The patient can remain anonymous and insert his letter into the note-book himself/herself. In order to give information about the note-book some posters have been hung on the walls of the department.

Results. The patients responded to the invitation to compile their own note-book in various ways: in some cases they handed in short sentences detailing their state of mind; in other cases they made long reflections on their cancer diagnosis and its effects on their lives; others wrote words of eulogy and thanks. One can perceive three states of mind: the first is one deep dejection, often linked to a negative attitude towards the illness, the cure, future itself; the second, conversely, is one of hope and optimism; the third is mixed, and juxtaposes hope and trust in the cure and the operators to the initial feelings of fear, panic and refusal. The word "cancer" is very rarely formulated, and is substituted by less alarming ones such as "illness" and "accident". Often family is cited as an important support to face the illness and the treatment.

Conclusions. The note-book for the patients represents an useful tool, not only for the patients themselves to give vent to sensations and states of mind, but also in order to gain a better understanding of their needs, which are often incompletely expressed by voice. Moreover, the reading of sentences rich with deep meaning exercises a deep emotive influence on the personnel, who discover in the reading not only the patients' poignant emotions but also their own. In other words, this initiative proposes once more the complexity of the relationships that come into being in such a delicate context as Oncology, in which circular relationships of great emotional impact and deep existential meaning come into being.

N10 PROJECT OF THERAPEUTIC EDUCATION FOR PATIENTS WITH CHRONIC MYELOID LEUKEMIA

Giaretto L., Fava C., Rege Cambrin G.

Medicina Interna II a indirizzo ematologico, Ospedale San Luigi Gonzaga, Orbassano, Torino

Introduction. Tyrosine kinase inhibitors such as imatinib and, more recently, dasatinib and nilotinib are oral medications that have many advantages over conventional chemotherapy for the treatment of chronic myeloid leukemia: greater specificity against tumour cells, less toxicity to healthy cells, greater efficacy, improved tolerability, ease of administration, possibility of home treatment, reduced access hospital. Nevertheless, the intake of these compounds in a total of less "controlled" may give rise to some difficulties in terms of patient adherence to therapeutic prescriptions. In light of the above was born the idea of implementing a therapeutic education project aimed at patients with chronic myeloid leukemia, which has as its main objective to improve adherence to drug treatment.

Methods. The patient education will be structured through a dialogue between health professionals and assisted and will be based on: a set consisting of information, tips, recommendations, use of appropriate media, after which the patient will become able to exercise self therapeutic competence that, in another context, would be the responsibility of health professionals.

Results. Through the development of specific communication skills, the operators can also contribute to improve quality of life of patients and their families, to increase the clinical assessment of patients by reducing complications, to promote a greater adherence to treatment and a more rational use of relevant services by users, to contain health care expenditure.

Conclusions. It is also very important that both patients and health professionals remain constantly vigilant to make sure that the drugs are given with the procedures and the schedule of the

treatment plan, to avoid that a failed or too nonchalant behavior nullifies all or part of the effectiveness of these compounds.

N11 NURSING MANAGEMENT IN TOXICITY DETECTION IN PATIENTS WITH CML (CHRONIC MYELOGENOUS LEUKEMIA)

Lionetti M.M.[1], Giaretto L.[2]

[1]Dipartimento di Oncologia ed Ematologia, SC Ematologia AOU San Giovanni Battista, Torino; [2]Medicina Interna II a indirizzo ematologico, Ospedale San Luigi Gonzaga, Orbassano, Torino

Introduction. This study is an example of how research can be potentially useful to improve the quality of nursing care, even in such a complex field as the one of oncohematology patient care.

Purpose. The purpose of this study was to encode an evaluation method in the management of adverse events; to make the results and toxicity comparable; to define the risk/benefit of the therapy and to pay more attention to the patient and his quality of life.

Materials and methods. The data about 306 patients with CML were reviewed in the period from February 2010 to February 2011. The toxicity was detected through a data sheet completed by the nursing staff after each outpatient visit made by each patient. The data were collected and processed in an appropriate database.

Results and conclusions. The average age of the patients is 57.8% M and 58.2% F, while the sex of the patients is 61% M and 38.2% F. The 29% of patients were enrolled in a clinical trial. The patients were taking the following drugs: 63.3% imatinib, 18.6% dasatinib, 14.3% nilotinib, 0.8% bosutinib. The major toxicities observed were of grade 1, including 88.8% fatigue, 5.88% diarrhea, 8.16% cutaneous rash, and were observed only one hematological toxicity of grade 4 and six of grade 3.

We can conclude that the knowledge of the most common symptoms associated to the disease or its treatment is critical for patient management, because it can cause particular suffering and can be source of morbidity, it can decrease the acceptance of treatment and worsen the overall quality of life. Nursing care in this area should aim at prevention, observation and early treatment of these complications. A good management of side effects is reflected in a better quality of patients' life. All information collected, the documentation and the comparison between people involved facilitate a better assistance.

N12 THE COMPUTERIZED MANAGEMENT OF DRUGS IN BAND H

Cullurà V., Invernizzi R.

USC, Oncologia DH e Ambulatorio, A.O. Ospedali Riuniti di Bergamo

In the National Health Service the H band is assigned to drugs in use only in hospitals.

These drugs can not be sold in public pharmacies, but they can be dispensed to citizens who are not hospitalized.

In the last few years the number of these drugs used for some cancer diseases has increased considerably.

In order to ensure the traceability of the prescription and of the delivery of these drugs in the outpatient department and in the DH, the corporate software for the prescription and the administration of treatment to hospitalized patients has been used.

When the patient goes to an outpatient visit or in DH, the doctor in charge of the outpatient department or of the DH, after visiting the patient, prescribes the same drug through FARMASAFE@ (corporate software) indicating the dosage, the number of tablets contained in a package, the daily dosage and the duration of treatment.

A printout of the prescription is given to the patient who then goes to the nurse's ancillary room for the withdrawal of the drug.

The nurse reads the prescription through FARMASAFE@ and records the delivery of the drug by reading the bar code of the package. In FARMASAFE@ the status of the drug changes from prescribed to delivered.

The delivery document of drugs in band H is printed in double copy through FARMASAFE@. Each copy is signed by the nurse in charge of dispensing the drug and by the patient.

A copy is given to the patient while the other one, together with the prescription, is attached to the outpatient report or the DH report.

N13 MANAGEMENT OF SKIN TOXICITY INDUCED BY CETUXIMAB: THE EFFICACY OF UREA AND VITAMIN K CONTAINING MOISTURE (VIGORSKIN®)

Tabellini E., Giuggiarini M., Fabbri M.A.

UOC Oncologia, Ospedale Belcolle, AUSL Viterbo

Background. Skin toxicity occurs in nearly 85% of patients treated with anti-EGFR monoclonal antibodies usually arising in the first 3 weeks of treatment. Our purpose was to evaluate the efficacy of a moisture containing urea and vitamin K (Vigorskin®) in the prevention and management of skin toxicity.

Methods. Ten patients affected with metastatic colon cancer treated with chemotherapy plus cetuximab were observed and monitored for skin toxicity. Vigorskin® was spread twice a day on the face, the neck and both hands and feet since the start of antineoplastic treatment. Skin toxicity was clinically monitored at every hospital admission and evaluated independently by physician and nurse. Compliance and efficacy of the moisture were explored. Main patients characteristics were: males = 7; females = 7; chemotherapy regimen: FOLFOX = 6 pts; FOLFIRI = 3 pts; irinotecan alone = 1 patient. All the patients received cetuximab at a standard dose together with chemotherapy.

Results. The median observation time was 5 months. All the patients were compliant to Vigorskin treatment. The appearance of skin toxicity was observed after a median of 4 weeks since the start of the treatment. The worst skin toxicity observed was of grade 2 (WHO) in 2 pts and characterized by acneiform eruption and painful fissures in hands and feet. All the pts presented grade 1 cutaneous xerosis and 1 pt had also a grade 1 acneiform rash and another one a grade 1 conjunctivitis. No grade 3-4 skin toxicity was observed. Moreover, an adequate control of itching and dry skin was reported. Even if not significant, our results compare favourably with those achieved in a historical control group of pts treated with nonspecific topical treatment in terms of delay and decrease in the severity of skin toxicities.

Conclusions. The availability of an effective topical treatment seems to reduce the velocity in appearance and severity of symptoms and is essential in order to increase compliance to cetuximab-containing regimens so avoiding the reduction of its efficacy.

N14 SKETCHES DEPICTING PATIENT-CAREGIVER RELATIONSHIPS

Tresoldi V.*, Bonetti L.*, Moleri C.*, Cabiddu M.°, Borgonovo K.°, Petrelli F.°, Olejnik K°., Barni S.°

**Psychoncology Service, Oncology Division, °Oncology Division, Azienda Ospedaliera Treviglio, Treviglio (Bergamo), Italy*

Drawing is one of the most important psychological projective tests which is able to "explore" the human personality. Pictures are the reflection of the interior world and they explain, without censorship, ones feelings, emotions and conflicts. (Ferraris 1974, Quaglia 2007).

Seventy-one couples, each consisting of an oncological patient undergoing chemotherapy and his caregiver, were asked to illustrate, by means of a sketch, their relationship, and in order to find the patient's coping strategies to undergo the Italian version of Mini-Mac (Grassi, 2005).

In 85% of couples both partners attempted to accomplish the same picture (cooperative pairs), while in 15% of samples one partner (in 88% of cases the caregiver) expressed an attitude of complete disregard for this task (non-cooperative pairs).

The quantitative analysis of the pictures showed that 33% of couples decided to represent their home and 30% of partners drew a self-portrait. In 82% of pictures there were positive natural elements such as sun (31%), trees (27%) or flowers (24%).

Although 94% of couples described their relationship as being satisfactory and supportive, in 53% of drawings the presence of disease was illustrated through projective elements such as clouds and mountains or verbal comments.

Patient prevalent coping style was reactive (60%).

In our sample pictures described a mainly positive realationship and the choice of these subjects seems to be linked up with a combative coping: the house represents the security of family life, and the sun the desire to face, with courage, the many difficulties.

In 80% of cooperative couples the patient's coping was combative and it seems to be linked up with the habit of the couple to share their tasks.

N15 GOOD CARE FOR CANCER PATIENTS

Bonetti L.*, Tresoldi V.*, Moleri C.*, Borgonovo K.^, Petrelli F.^, Cremonesi M.^, Cabiddu M.^, Olejnik K.^, Barni S.^

**Psychoncology Service, ^Oncology Division, Treviglio Hospital, Treviglio (Bg)*

Good care offered to cancer patients has an important impact on their satisfaction and quality of life.

The aim of this study was to analyse the satisfaction of patients concerning the care they received.

Sample consisted of 110 patients undergoing chemotherapy (20 males, 90 females, mean age 52 years, range 28-75).

The short version of the WHOQOL test (Murphy, 2000) was administered to assess their quality of life.

Patients were asked to undergo a semistructured psychological interview to determine their degree of disease awareness and to collect their opinions concerning the ability of doctors in communicating bad news and explaining therapies. A 6-point Likert scale (1: dissatisfied, 6: satisfied) was used.

Most patients were fully aware of having cancer (97%) and 75% of the sample had an acceptable quality of life. They received comprehension and support from their oncologist and recognized his ability in disclosing bad news.

The media score was 5.38: 61% was completely satisfied, (score 6), and 28% gave a score of 5. Dissatisfaction concerning information and care received was expressed by a minority of patients, a score of 3 or 4 being given by 8% of the sample and a score of 1 or 2 being given by 2%.

No correlation was found between satisfaction and other variables which were related to age, sex, education, job, civil status or disease awareness.

The only correlation found was that between satisfaction and quality of life.

Most patients were satisfied with the detailed information provided and the concise way in which it was given.

Patients emphasised their experience of good care and it appeared to be linked up with a good level of their quality of life.

It is possible that the satisfaction of patients and their good quality of life are due to the presence of the Psychoncology Service in the Division which offers help to the medical staff in communicating bad news.

N16 RELATIVE ISSUES TO INFORMED CONSENT IN PRACTICE ONCOLOGY

Chilelli M.G., Moscetti L., Nelli F., Padalino D., Signorelli C., Primi F., D'Auria G., Fabbri M.A., Ruggeri E.M.

Oncology Unit, Belcolle Hospital, Viterbo, Italy

Background. Although the informed consent has been discussed, some questions have not been completely clarified.

Method. The purpose of the report is to provide answers to some questions frequently asked in practice oncology.

Discussion. To demonstrate the acquisition of the consent should we obtain more than the form sign?

The answer is yes for the following reasons: the filled-in form is not interactive, the terminology used is not generally suited to each patient, cannot anticipate every possible situation or adverse event. Trick can be used in the immediate future: acquisition of consent by two doctors with involvement of a person indicated by the patient, possibility to integrate the form with further information, even in the following days. Possible future trick: registration of the conversation.

As far as informing the patient with poor education and how? Providing for more interviews, providing gradually information with simple terminology. How do we inform the patient who wants to be informed? The patient should be necessarily informed in order to obtain a valid consent related to the management of patient's disease. How to behave about the excessive patient's expectation in care? It is necessary that the physician carry-overs with caution, on a plan to balance, the expectations of the patient. How to inform the patient already treated at another cancer unit, just informed of this illness and the purpose of care? We need to give the correct information in accordance with the recommendations of the code of medical ethics. How to avoid the conflict with the members of the family of the patient who are insisting on not informing him? It should be put in place every action of conviction of the members of the family, in order to obtain the cooperation of the same, necessary during the diagnosis, therapy and palliative care.

Conclusion. The acquisition of informed consent should be implemented in order to obtain an effective full patient understanding and physician safeguard.

N17 THE ELDERLY: INCREASING POPULATION IN ONCOLOGY, A "NEW" COMMITMENT TO THE NURSE. ANTIBLASTIC INTRAVENOUS THERAPIES, BENEFITS AND DIFFICULTIES: THE EXPERIENCE OF A DAY HOSPITAL

La Rocca R., Licciardello P., Di Mauro G., Scandurra G., Taibi E., Sanò M.V., Alì M., Chiarenza M., Aiello R.A., Caruso M.

UF Oncologia Medica, Humanitas Centro Catanese di Oncologia, Catania

Background. In the past, elderly cancer patient, simply for age reasons, was barred from access to effective treatment such as chemotherapy. Today, we are witnesses to an increase of cancer and related co-morbidity in this patient group. As a result, the nurse's role becomes one of simultaneously addressing problems both oncological and geriatric in the management of intravenous antiblastic therapy and in their educational role.

Proposal. Assessing the importance of the nurse in reducing the time of medical evaluation and highlighting specific issues to antiblastic intravenous therapy in elderly through questionnaires aimed at assessing the patient's self-sufficiency in ADL (Activity of Daily Living) and IADL (Instrumental Activity of Daily Living).

Materials and methods. A sample of 154 patients was analyzed in the years 2008-2010. Seventy-eight F and 76 M aged 70-86 years (median 75), 15 were older than eighty years. The treatment setting was: 25 in adjuvant and 129 in metastatic - treated with intravenous therapy and diagnosed with different forms of cancer. During the first contact, the nurse gives to all patients the ADL and IADL questionnaires and in the meanwhile makes additional assessments through clinical observation and simple verbal questions.

Results. The nurse through the questionnaires: reduces the time to conduct the geriatric assessment of elderly cancer patients, determines the degree of patient autonomy and coordinates with caregivers all the therapies' side effects.

If the administration of intravenous antiblastic therapy allows for absolute compliance to the dosage at the same time involves a number of difficulties such as finding a venous access and an absence of reaction in case of extravasation.

Conclusions. In our experience, relying on the role of the nurse administering the above mentioned tests maximizes time of evaluation and also monitor patients' mood, as the elderly cancer patient feels the need to "create a relationship" and be able to trust the others. Often only the nurse can establish a relationship of this type with the patient and his family.

N18 INTRAVESICAL CHEMOTHERAPY: A SIMPLE NURSING PROCEDURE OR A CHALLENGE IN THE MANAGEMENT OF A COMPLEX SITUATION? A DAY HOSPITAL EXPERIENCE

Licciardello P.[1], Todaro F.M.[1], Di Mauro G.[1], Scandurra G.[1], Alì M.[1], Taibi E.[1], Fallica G.[1], Miano E.[1], Costantino G.[2], Aiello R.A.[1], Caruso M.[1]

[1]UF Oncologia Medica, [2]UF Chirurgia Oncologica, Humanitas Centro Catanese di Oncologia, Catania, Italy

Introduction. About 80% of urothelial cancers are defined as superficial tumours. A bladder instillation with BCG or other chemotherapy should be required following the endoscopic surgery to prevent the disease. Although this procedure has less toxicity than systemic chemotherapy, it has serious psychological consequences for the patient, mainly related to sexual and social life. The nurse who provides the administration of the drug, thanks to the privileged position of closeness and intimacy, can be responsible for the education of the patient, making better compliance to the treatment, alleviating psychological distress and denying many "superstitions".

Proposal. Evaluating the role of the nurse in the study of psychological distress, administering questionnaire and contributing to the patient education.

Materials and methods. Ninety-eight patients (median age 72 yrs, range 39-93) were treated (2008 -2011) (F 13/M85) with BCG, MITOC, EPI and GEM. The procedure consists of the insertion of a catheter into the bladder to drain it, under sterile conditions, to avoid traumatizing the mucosa, infusing the suspension slowly and then removing the catheter. The patient can go home, but must still retain the drug for 60 additional minutes for a total of 2 hours. At the end patients should urinate sitting down for safety reasons.

Results. In our experience just a few patients agreed to answer questions concerning sexual life for low educational level, age or decency: these assessment tools are less suitable in this subgroup of subjects. It has been much more useful talking to reassure the patient about the possibility of venereal cancer transmission, training to dispose urine in the hours following the therapy, and the need for increased hydration and hygiene requirements in married life. The closeness with the nurse was vital to overcome the trauma related to the disease and surgical procedures.

Conclusions. The role of the nurse in the management of bladder cancer patients treated with intravesical chemotherapy is vital to improve patient compliance and reduce fears.

N19 STREAM: A SUCCESSFUL PROJECT TO COORDINATE MEDICAL AND NURSING MANAGEMENT OF SKIN TOXICITY IN PATIENTS WITH HEPATOCELLULAR CARCINOMA AND METASTATIC RENAL CELL CARCINOMA TREATED WITH SORAFENIB. EXPERIENCE OF A DAY-HOSPITAL

Todaro F.M., La Rocca R., Licciardello P., Di Mauro G., Mazzamuto L., Alì M., Scandurra G., Aiello R., Miano E., Caruso M.

UF Oncologia Medica, Humanitas Centro Catanese di Oncologia, Catania, Italy

Introduction. Sorafenib is an oral small molecule multi-targeted agent indicated for the treatment of patients with hepatocellular carcinoma and advanced renal cell cancer. The most frequent side effects of sorafenib are: rash (34%), hand foot skin reaction (HFSR) (27%), diarrhea (33%) and hypertension (11%). The novelty brought by the drug requires a multidisciplinary

team approach. In particular, thanks to the direct interaction with the patient, the nurse providing the skin care kits can be responsible for the education of the patient, improving in this way the compliance to treatment.

Proposal. To evaluate the value of the integrated management of skin toxicities, and the effectiveness of a specific dermatological kit, in improving compliance to treatment and reducing treatment interruptions and severity of skin toxicities (as perceived by the patient).

Materials and methods. Between 11 May 2010 and 28 February 201, sorafenib was administered to 15 (3F/12M, median age 72 years; range 46-79 yrs) 7 affected by kidney cancer and 8 by hepatocellular carcinoma.

The nurse provided a dermatologic skin care kit. Cutaneous toxicity was evaluated by collection of images, clinical data and completion of a questionnaire answered by the patient at baseline and during the treatment period.

Results. Only 2 patients out of 15 interrupted the treatment due to HFSR CTC grade 2. Generally, instructions for the application of the dermatological products were necessary, and this ensured their correct use. Increased visit frequency (every 10-15 days) resulted in a reduction of the HFSR symptoms. This kind of approach had a double benefit for the patients: relievement of pain and emotional wellbeing through a perceived better care. The questionnaires have highlighted the importance of the active role of the nurse in the management of skin toxicities.

Conclusion. The integrated medical nursing care was successful in the prevention and control of sorafenib cutaneous toxicities resulting in fewer treatment interruptions, and lower severity of symptoms. Quality of life was improved and psychological relief was perceived by the patients.

N20 MOLECULAR TARGETED DRUGS AND NEW TOXICITIES. WHEN CANCER TAKES YOU AWAY EVEN YOUR IDENTITY. HOW CAN NURSES RELIEVE RASH DISTRESS DUE TO ANTI-EGFR MONOCLONAL ANTIBODY TREATMENT ? A CONTINUING EXPERIENCE

Di Mauro G., Todaro F.M., Licciardello P., La Rocca R., Scandurra G., Clementi S., Miano E., Aiello R.A., Caruso M.

UF Oncologia Medica, Humanitas Centro Catanese di Oncologia, Catania

Anti-EGFR monoclonal antibodies are targeted therapies who inhibit cancer growth by interacting with specific molecules involved in cell signaling pathways.

In our institution experience, since March 2006 to April 2011 we treated 80 patients with cetuximab (colorectal or head-neck cancer) and 15 patients with panitumumab (colorectal cancer) and one of the most disabling side effects, mainly psychological, is cutaneous rash.

Rash can spread on face, especially cheeks and chin, back or nails. Sometimes desquamation involves eyebrows and scalp too. Patients experience difficulties in relating to other people, they feel diverse, shame and don't accept such a "new face". The fear of judgment makes patients lonely and confined at home.

The nurse's role is helping patients in providing a continuous physical and mental support.

Nurses are the best in encouraging and giving advices (some clever devices can be useful to relieve the unpleasant sensation of itch, sting and skin tension: for example, moisturizing creams or body lotions to mitigate desquamation, wearing large cotton clothes avoiding synthetics, decongestant product such as mentholated talcum and avoiding prolonged sun exposure) to patients. In addition, patients can draw conclusions about the hospital and the team care.

The main purpose of our team is to make the targeted therapy more tolerable to patients by explaining them that all disturbs are reversible and how to alleviate them.

In our experience the nurse is considered as a close friend to the patient, always reliable to listen and understand patients' sufferings providing physical and psychological comforts. Our aim is to reach an holistic approach to oncological cares that makes the patient feel at home.

N21 THE FOLLOW-UP ISSUES: FROM THE NECESSITY TO THE OPPORTUNITY

Brandi G.[1], Nannini M.[1,2], Longobardi C.[1,2], Maleddu A.[1,2], Saponara M.[1,2], Di Tullio P.[1,2], Degli Esposti C.[1,2], Katzinas J.[1,2], Di Girolamo S.[1,2], De Rosa F.[1,2], Agostini V.[1,2], Macchini M.[1,2], Rubino D.[1,2], Pini S.[1,2], Pallotti M.[1,2], Paragona M.[1,2], Lolli C.[1,2], Corbelli J.[1,2], Garajovà I.[1,2], Vecchiarelli S.[1,2], Mandrioli A.[1,2], Zucchini G.[1,2], Pantaleo M.A.[1], Di Marco M.[1], Cucchetti A.[3], Biasco G.[3]

[1]Department of Hematology, Oncology and Laboratory Medicine, [2]School of Specialization of Medical Oncology, University of Bologna, Bologna, Italy; [3]Interdepartmental Center for Cancer Research "G. Prodi", University of Bologna, Bologna, Italy

Background. According to the new formative plan of School of Specialization in Medical Oncology (defined by DM 2006), the follow-up examination should be autonomously conducted by the fellows who are in the last year of study. However, the surveillance programs remain unsettled and represent by now a widely debated argument, due to the lack of unanimous guidelines, as well as the different attitude of patients and clinicians towards the follow-up. Therefore from the educational necessity of well defined surveillance programs, we take the opportunity to revise the literature on this topic in order to elaborate a manual which can be applied in clinical practice.

Methods. We reviewed the scientific literature on the follow-up strategies of the most tumour diseases (colon, rectal, breast, anal, pancreas, thyroid, head-neck, bladder, renal, uterine, stomach, lung and oesophagus cancer, melanoma, HCC, cholangiocarcinoma, sarcomas, GIST, NET and resected colorectal liver metastases) focusing on the following aspects: the clinical rationale of the follow-up according to EBM analysis, the main international guidelines, procedures and costs.

Results. We found that for most diseases an unanimous follow-up strategy, in terms of modalities, intensity and duration, is lacking and the surveillance programs are based on expert's opinion. For each disease we reported a personal proposal of surveillance according to our institutional experience combined with the main international guidelines, with an educational intent addressed to the fellows of School of Specialization in Medical Oncology.

Conclusions. The educational necessity of well defined surveillance programs for the most frequent cancer diseases has led us to revise the literature on this topic up to elaborate a manual

which can be applied in clinical practice. The collection of homogeneous clinical data will allow to conduct perspective studies on large series, in order to clarify the usefulness of the follow-up programs in terms of costs and benefits. Literature data analysis through a Markov simulation model will be performed for evaluating the cost-effectiveness of each follow-up strategy.

N22 A LETTER FROM A DYING WOMAN - A MESSAGE FROM THE OTHER SIDE OF THE "WALL OF SILENCE"

D'Alessandro V., Freda M., Boragine R., Cela P., Di Giorgio A., Piscitelli A.P., Giannolo A., Vendemiale G.

Respiratory Oncology Section, I Internal Medicine Department of IRCCS "Casa Sollievo della Sofferenza" Hospital, San Giovanni Rotondo (FG), Italy

Background. To communicate the diagnosis of tumour is not easy, especially if the diagnosis is lung cancer. The patient's family very often asks us for not communicating the true diagnosis to the patient, for fear of a consequent strong depression. Between sick and relatives the communication becomes difficult, determining the so-called "conspiracy of the silence". Aim of our work is to improve the communication within the family.

Methods. We have used a letter appeared in 1998 on an Italian magazine, *Famiglia Cristiana*, n 39. In this letter a female sick of tumour affirms that the matter of the "truth to the sick" is a forgery problem, since the tumour patient often knows the truth, even if the patient makes as if nothing happened, and that is the sick, for the most part, to have to protect the relatives from the news of the illness. The letter was handed to the family when they asked for not communicating the true diagnosis or when they expressed problems in communication of the diagnosis to these patients. Together with the letter it was given a questionnaire that aims to appraise the difficulties of communication between the sick and his or her family and if the letter has improved somehow such difficulties.

Results. Between 2005 and 2010 we gave 105 letters and questionnaires to families of hospitalized patients in our department. Before receiving the letter, only in 7% of the cases the family had openly talked about the diagnosis of tumour to one's own relative. The 75% of relatives declared very useful the reading of this letter. The 69% of family members believed that general communication with their relative improved and in 55% of the cases they succeeded in speaking more openly about the illness with their sick relative.

Conclusion. To take over some time and also giving a simple letter to the family can improve the communication between the cancer patient and his family.

N23 AN OBSERVATIONAL TRIAL: THE MANAGEMENT OF PORT-A-CATH (CENTRAL VENOUS ACCESS SYSTEM) IN CANCER PATIENTS AND NOT, AT THE "AZIENDA OSPEDALIERA BOLOGNINI DI SERIATE"

Iaculli A., Galdy S., Cotroneo G., Rodà G., Duluc M., Galmozzi A., Nastasi G.

Azienda Ospedaliera Bolognini, Seriate

Background. The use of central venous access systems is very common in medicine and especially in oncology. The main indications are: chemotherapy regimens continuously infused, administration of vesicant drugs, hydration and parenteral nutrition, pain management with infusion pump systems, recovery of venous access in patients with poor vascular bed, central venous pressure monitoring, etc. Nowadays, several types of central venous catheter (CVC) are available with different characteristics. The CVC may lead to various complications in the short and long term, however, few data are available in the literature especially with regard to the incidence of infections and thrombosis. The PORT-a-Cath is as safe as it is a totally implantable device. It consists of two main components: reservoir and central venous catheter.

Aim. The main purpose of this perspective no randomized trial, that was initiated on 1 January 2011, was the creation of a care pathway for positioning, management and removal of each PORT-a-Cath. The objectives of this study are represented by: 1) recording the number of PORT-a-Caths implanted in our hospital *per* year; 2) percentage of infections, thrombosis, adverse reactions/ulcerations, device malfunctions or any other complications *per* each 1000 days of device-implantation; 3) improving information and training for each patient.

To achieve this goal we created a database (the data will be collected every three months with an initial analysis performed after 1 year of monitoring) and we elaborated a notebook to give to each patient. Eventually, it will be considered the opportunity to build a management algorithm for each complication.

Conclusions. With our study we want to identify patients who deserve the placement of a central venous catheter such as Port-a-Cath, improve the management of the device and provide valid indicators of quality.

N24 NURSING MANAGEMENT OF SKIN TOXICITY DURING CETUXIMAB THERAPY

Di Leo L., Stefanelli A., Colombo D., Rossi B., Rubino N., Borghi M., Kuzhuppil T., Cattaneo M.T., Filipazzi V., De Troia B., Farè E., Vimercati S.°, Curcio R.°, Fasola C., Ferrario S., Gambaro A., Tosca N., Isabella L., Damiani E., Piazza E.

Oncology Department and °Pharmacy, "Luigi Sacco" Hospital, Milan, Italy

Background. Cetuximab is a monoclonal antibody against the epidermal growth factor receptor (EGFr). It has shown activities against advanced colorectal cancer, head and neck carcinoma but it often causes skin toxicity. This peculiar toxicity is related to the inhibition of EGFr in the skin, which is crucial for the normal development and physiology of the epidermis. Preclinical data suggest that topical application of a potent phosphatase inhibitor menadione (vitamin K1) can rescue the inhibition of EGFr. Recently a specific cream is disposable for treatment and prevention[1]. Aim of nursing care is to evaluate the toxicity before it may cause significant physical and psycho-social discomfort.

Material and methods. We have reviewed local practice of skin toxicity management during treatment with cetuximab. From October 2010 the new patients with metastatic KRAS WT colorectal cancer were treated with cetuximab at a dose of 250 mg/m^2 weekly in combination with FOLFIRI chemotherapy. They were treated with t.i.d topic VigorskinK1 cream to prevent skin rash. They were followed up during chemotherapy at least 6 months, once a week. Skin toxicity was evaluated according to NCI CTCAE and matched with the other pts treated with cetuximab before the use of vitamin K1.

Results. Of 45 patients treated before October 2010 we record mild skin rash (G1) in 30%, moderate (G2) in 20% nd severe (G3-G4) in 40% and many of these patients discontinued cetuximab therapy for toxicity. Since this date we treated 14 new patients. They were 5F + 9M, median age 62 years (range 51-77), cetuximab was performed as first-line chemotherapy in 4 pts and second-line in 10 pts. Vitamin K1 was used as topic application from starting CT in 12 pts while in 2 cases it was associated with chemotherapy 2 months later. We record G1 toxicity in 22%, G2 in 16%, G3 in 30% while 32% didn't show any toxicity. Only 1 pt has interrupted the treatment; six times it was necessary a systemic therapy with oral tetracycline in three patients. The acneiform eruptions were confined to seborroic areas as face and thorax (64%); xerosis developed at the fingers, palm and soles associated with painful fissures (22%). Less frequently, pruritus, dry skin, desquamation, conjunctivitis, paronychia were observed. Ten pts are under chemotherapy with cetuximab also because of their objective response.

Conclusions. The goal of managing EGFr inhibitor-associated skin toxicity is to minimize the detrimental effects of the rash on patients' quality of life and treatment course without antagonizing the clinical efficacy of EGFr inhibitors. In our experience educational nursing management and vitamin K1 are efficacious to prevent epidermal toxicity during cetuximab therapy.

References

1. Ocvirk J: Treatment of cetuximab-associated cutaneous side effects using topical application of vitamin K1 cream. J Clin Oncol, 7 (20): e15087, 2009.

N25 IPILIMUMAB ADMINISTRATION TO METASTATIC MELANOMA PATIENTS IN THE DAILY PRACTICE: NURSING MANAGEMENT IN THE OUTPATIENT SETTING

Iacovelli A., Piccinelli M., Resti M., Speranza S.

Medical Oncology and Immunotherapy, Azienda Ospedaliera Universitaria Senese, Siena

Background. The anti-CTLA-4 monoclonal antibody ipilimumab prolongs survival of metastatic melanoma (MM) patients (pts). Inhibition of CTLA-4 can generate a well defined syndrome of delayed auto-inflammatory side effects named "immune-related adverse events" (irAEs), which are generally reversible and manageable. This study aimed to evaluate the feasibility of ipilimumab administration to heavily pre-treated melanoma pts in an outpatient setting.

Methods: Fifthy-five pts (30 males, 25 females), median age 57 (23-87), ECOG performance status 0-1, median 3 (1-5) prior therapies for MM, received ipilimumab within an Expanded Access Program at 3 mg (28 pts) or 10 mg (27 pts). Ipilimumab was administered at 3 mg/kg i.v. over 90 minutes (min), q 3 weeks (wks) for 4 cycles or at 10 mg/kg i.v. q 3 wks for 4 cycles and q 12 wks in the maintenance phase, after a 12 wks rest. At each administration pts received prophylactic i.v. anti-histaminic and underwent assessment of vital parameters including blood pressure, heart rate and body temperature at baseline. These were re-evaluated at 5, 30, 60 and 90 min during ipilimumab administration and 90, 120, 150 and 180 min after the end of treatment.

Results. A total of 278 infusions (100 and 178 at 3 and 10 mg/kg, respectively) of ipilimumab were administered. None of the pts manifested acute AEs, such as pruritus, flushing, hypotension, vomiting and anaphylactic shock that required treatment or hospitalization. No clinically meaningful changes in vital parameters occurred. One patient, experienced fever with chills, 30 min after the end of the 2nd ipilimumab (3 mg/kg) infusion, which resolved within 1 hour with i.v. paracethamol; noteworthy, no adverse reactions were recorded for this pt with subsequent administrations of ipilimumab.

Conclusions. Infusion-related acute reactions to ipilimumab administration are highly uncommon. Ipilimumab administration at 3 and 10 mg in an outpatient setting is a feasible approach also in heavily pre-treated melanoma pts and it does not require extensive monitoring of vital parameters.

N26 NURSE DRIVEN TRAINING OF OUTPATIENTS RECEIVING CAPECITABINE FOR COLORECTAL CANCER: PRELIMINARY RESULTS FROM A SINGLE INSTITUTION EXPERIENCE

Demichelis M.M., Crocetti C., Lombardi P., Tropeano M., Ponzetti A., Spadi R., Fora G., Pinta F., Fanchini L., Ciuffreda L., Racca P.

ColoRectal Cancer Unit, Medical Oncology 1, Hematology and Oncology Department, A.O.U. San Giovanni Battista, Turin

Background. The continous development of oral chemotherapic drugs has increased the need of an outpatient approach capable to manage the clinical complexity of patients receiving them.

Methods. We report the early experience of the capecitabine outpatients clinic at Colorectal Cancer Unit in Medical Oncology 1 division in San Giovanni Battista hospital, Turin.

At the fisrt access a nurse carried out a counseling in order to educate patients about the expected toxicities and the first approach to them. During the following visits the nurse reported the toxicities according to CTCAE version 3.0 and provided first-line counseling. Patients and caregiver acquired capabilities and compliance to the prescribed schedule were evaluated using a purpose-made checklist. Patients and caregiver not reaching a minimum level of comprehension and ability in toxicity management underwent a further training by nurses team. Data about patients satisfaction were also collected.

Results. In the first months of 2011, 115 consecutive patients treated with capecitabine based scheme for colorectal cancer (CRC) were trained. Fifty-seven percent were female with a median age of 65 years (range 34-87). Twenty-five percent of patients and caregivers needed nurse re-training about general management, 9% about adequate dosing, 18% about identification of adverse events and 20% about early management of toxicities. At a final evaluation all patients reached a basic training level.

Conclusions. In our experience a multistep patient and caregiver training operated by nurse was able to improve their compliance and awareness of an early identification and correct management of capecitabine-induced adverse events.

N27 A PHARMACIST IN THE ONCOLOGY DEPARTMENT: REAL CHANCE?

Lebboroni M.[1], Berti G.[2], Cestaro F.[1], Pessa S.[1], Rosti G.[1]

[1]Department of Oncology ULSS 9; [2]Department of Pharmacy ULSS 9, Treviso

Introduction. In the Italian health system characterized by a frenetic introduction of new, high cost, disease-specific and critical management molecules, the department of Oncology in Treviso joined a pharmacist in his team to improve the quality of health services and maintaining, at the same time, a reasonable cost: this profession has the aim of combining health needs with those of sustainability. The pharmacist was able to intervene in many aspects related to the drug, not only from a management and economic point of view (Pharmacoeconomics), but also patient-oriented (Pharmaceutical Care) improving his clinical pathway (Clinical Governance).

Materials and methods. Cooperation between department of Pharmacy and department of Oncology has led to the definition of a priority scale to work on: pharmaceutical expenditure containment, risk management, centralized cytotoxic preparation.

Activities:

- monthly assessment of drug consumption;
- planning and budgeting;
- reviewing the drug logistics;
- reviewing therapy protocols by multidisciplinary group in accord with international guidelines;
- reducing costs, cytotoxic waste and his correlated risks buying cytotoxic drug bags, generic and biosimilar drugs and rationalizing the doses;
- creation of paths to drug distribution;
- rationalization of daily preparation (drug day);
- monitoring and supporting doctors during compilation of national and regional registers.

Results. After six months we can say that the impact of this project involved the following areas:

- assistance: realization of a complete service to the patient;
- logistics: reallocation of resources assistance;
- economics: reduction of expenditure. Comparing costs of the 1st quarter of 2010 with those of the 1st quarter of 2011 we can observe a reduction of about € 350,000 from € 1,950,000 to € 1,600,000.

Conclusions. The multidisciplinary group results (pharmacist, clinicals and nurses) demonstrate the usefulness of introducing, in many clinical departments, the pharmacist: a figure different from the common stereotype of "the one who controls" but as an opportunity to optimize the business' accessibility to drugs, ensuring a balance between demand and sustainability.

N28 ADDRESSING THE UNVOICED NEEDS OF CANCER PATIENTS (CP)

Cristina G., Gareri R., Capomolla E., Ricciotti M.A., Benedetti I., Gullo B., Montemurro G., Felicetti V., Cifaldi L.

U.O.C. Oncologia Medica, Azienda USL RM G, Ospedale Parodi Delfino, Colleferro, Rome, Italy

Background. The CP has specific needs, both implicit and explicit, of which doctors and nurses have to be aware, calibrating their own relational modalities regarding a disease that continues to terrorize.

With the development of more effective cancer disease treatments, the disease management styles, knowledge and their impact on quality of life and assistance environment have become increasingly important.

Aim. Being aware that patients' satisfaction is a priority and to meet their needs a specific questionnaire was developed.

Methods. CPs with solid tumour receiving adjuvant or metastatic treatment were asked to fill in the questionnaire, divided into ten questions, covering: physician-patient communication, patient's psychological state, patient's expectations of medical/nursing staff. All patients met the criterion of awareness about their disease.

Results. 210 patients (107 males, 103 females; age 67.5±12.2 years) voluntarily partook and returned the questionnaire. CPs majority filled in all the questionnaire items. In brief: the patient's awareness and acceptance were investigated by two questions "Do you feel satisfied with the information received in this department during your recovery?" and "Do you feel pleased with the reception in this department?" CPs responses to both questions revealed that they were fully satisfied.

Remarkable were the answers to the question: "How do you feel during therapy?" 160 out 210 CPs reported they felt at ease during the course of therapy.

To assess the patient's subjective perception regarding the communication and health care provided by the staff, it was asked "Do you feel anxious?" 105 out 210 CPs reported to be anxious.

Discussion. The analysis of data collected through the questionnaire reveals some essential reflections on the importance of the relational dimension in the context of oncological disease which invests the medical/nursing staff. This is to lessen the stress level caused by the illness and its healing process. The survey helped us to define the CPs' expectations. Following these results, volunteer psychologists were accepted in the department to assist CPs and their relatives.

N29 TOTALLY IMPLANTABLE CENTRAL VENOUS ACCESS: PATIENT AGREEMENT IN A SINGLE UNIT

Cavarra M., Pommella C., Violante S., Russo S., Verani S., Sarandrea C., Buconovo S., De Carli R., Scoppola A., Marchetti P.

Oncologia, Istituto Dermopatico dell'Immacolata, Roma

Background. Totally implantable venous access port systems have several advantages over externalized indwelling catheter systems, including fewer restrictions on activities such as bathing, and a low incidence of infection. We conducted a study to examine the impact on quality of life of patients with totally implantable central venous access.

Patients and methods. We examined 125 patients, with a variety of solid neoplastic diseases requiring chemotherapy who were undergoing placement of implantable central venous access, observed at Day Hospital of Oncology of Istituto Dermopatico dell'Immacolata in Rome, during a period of approximately 3 months. The anonymous questionnaire, containing 17 items, was administered on the flush of port-a-cath with heparin, after conclusion of endovenous chemotherapy. The questionnaire measured physical and psychologic wellbeing and the impact on quality of life of those patients who, after completion of therapy, retained their ports for extended periods of time.

Results. 125 patients (92 F, 33 M), median age 66 years (range 25-84) were enrolled. The median time of implant of central venous access was 24 months (range 3-108). The oncologist prescribed the implant of port more often than nurse (93% vs 5%). A total of 122 (97%) were well informed about the advantages and disadvantages of the central venous access and only 16 (13%) patients had doubts about the implantation of

port. Fewer (5%) patients had severe restriction on daily activity and had pain related to port (14%). The majority (70%) of patients remembered the period of the chemotherapy through the port-a-cath and a half of patients (52%) would remove the port. A part of patients (21%) felt the stress of the flushing to maintain patency of port-a-cath but the majority of them liked the quality of nursing service.

Conclusion. The port-a-cath was safe and effective and had no detectable impact on daily activity but a half of patients would remove the port in a short time because of flushing-related discomfort and disease-anxiety.

N30 ADRs: RESULT OF PHARMACIST AND ONCOLOGY COOPERATION

Ghiotto E.[2], Lebboroni M.[1], Cestaro F.[1], Berti G.[2], Rosti G.[1]

[1]Department of Oncology, [2]Department of Pharmacy, ULSS 9, Treviso

Introduction. Adverse drug reactions (ADRs) are one of the main public health problems, having significant consequences of both clinical and socio-economic type, as lower quality of life, increased and prolonged time of hospitalization and rise of mortality. Pharmacovigilance is a simple tool that allows to collect important drug safety signals, particularly brand new molecules, and to create a network of national and international community.

Materials and methods. Every report of suspected ADRs in Treviso was collected and analyzed in a period from January 2008 to April 2011, evaluating especially those from the department of Oncology, because, since November 2010, there's a pharmacist in Oncology's equipe.

Ones below are evaluated:
- total ULSS N.9 reports;
- total Oncology's reports;
- warned drugs;
- severity of reactions;
- gender and patient's pathologies;
- doctor's name.

Results. Department of Oncology has been for many years the leading reporter in hospital (63% of total reports); in fact in the last two years were sent about 20 warnings/year. It's important to note that in the first four months of 2011 there was an increase of:
- reports in comparison with the totality of hospital's reports and the previous years: 10/14 while in 2008 10/18, 2009 17/30, 2010 23/33;
- reports of serious or potential injury in comparison with previous years: 50% (1 death and 4 serious situations) while in: 2008, 10%, 2009, 41%, 2010, 35%;
- reports about "old" drugs such as docetaxel and paclitaxel, and not about innovative drugs: 70% while in 2008, 20%, 2009, 53%, 2010, 52%;
- reports (serious and not serious) about women with breast and ovary cancer: 70% while in 2008, 20%, 2009, 47%, 2010, 48%.

Conclusions. Results of collected data reveal that most of ADRs are caused by older drugs and not innovative ones. Having a pharmacist in the oncology's team has provided useful support for the identification of suspicious reactions (because they are particularly serious and/or unexpected) and, also, for completing and forwarding the report.

N31 FEASIBILITY OF PATIENTS SELF ASSESSMENT WITH NURSE SURVEILLANCE IN THE MANAGEMENT OF SUNITINIB-RELATED TOXICITY IN METASTATIC RENAL CELL CARCINOMA

Sacco C., Costantini P.*, Miscoria M., Rihawi K., Ermacora P., Donato R.*, Andreetta C., Bin A.*, Fasola G.

Dipartimento di Oncologia, Azienda Ospedaliero-Universitaria, Udine, Italy
**Nurse*

Aim. The introduction of oral anticancer drugs in clinical practice has changed patients' and toxicities' management. We previously reported (Costantini P. et al., Ann Onc, 2009) that nurse phone-based surveillance can reduce the occurrence of sunitinib-related toxicities and hospital admissions. Following this experience we conducted an observational study on sunitinib-induced toxicities combining self patient assessment with nurse surveillance.

Methods. All patients receiving sunitinib for metastatic renal cell carcinoma at our center were included. At the time of the first visit, the patient received complete information on sunitinib-related toxicities both from the doctor and the nurse who deals with the patient, and was invited to fill in a daily check-list. Aim of the study was to prevent or limit grade >2 side effects and to manage minor side effects at home. The check-list was written in non-technical words to be easily understandable and included the following questions: 1) Has your blood pressure ever been over 150/90? 2) Have you ever had >4 episodes of stool loose per day? 3) Have you ever had "burning-aching" mouth that prevented you to have a meal? 4) Have you ever noticed blisters on your feet or felt hurting soles or hands? If the answer was yes in any question, the patient was invited to call the hospital and talk to the dedicated nurse. Compliance to treatment, incidence and grade of toxicities were recorded.

Results. Between May 2010 and May 2011 we enrolled 22 patients (median age 65 yrs, range 61-75). Total number of cycles was 54 with a median dose per cycle of 50 mg on a 4/6 weeks schedule. Overall 20 phone calls were received for grade 2 side effects: 7 hypertension, 4 diarrhoea, 5 mucositis, 2 HFS. No grade 3 or 4 toxicities were recorded. Most toxicities were managed at home with nurse advices; only patients experiencing hypertension required medical visit. Unplanned hospital admissions have not been observed.

Conclusions. Patient self-assessment and phone-based nurse surveillance is a feasible modality to limit toxicities in patients treated with sunitinib. This strategy may help to prevent the occurrence of severe toxicities of this drug, improving compliance and reducing hospital admissions. We are using the same surveillance to monitor toxicities in patients on everolimus and sorafenib treatment. Data will be presented at the meeting.

N32 SINGLE INSTITUTION EXPERIENCE WITH APREPITANT FOR PREVENTING CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING

Reale S.[1], Stabile C.[1], Mazzola A.[1], Ragusa R.A.[1], Longo F.[1], Antinucci S.[1], Agozzino R.[1], Sanfilippo G.[1], Rao M.S.[2], Chiarenza M.[1], Di Marco R.[1], Scandurra G.[1], Carillio G.[3], Caruso M.[1]

[1]Humanitas Centro Catanese di Oncologia (CCO), Department of Medical Oncology, Catania; [2]Humanitas Centro Catanese di Oncologia (CCO), Department of Psycho-Oncology, Catania; [3]Azienda Ospedaliera Pugliese-Ciaccio, Department of Oncology and Hematology, Catanzaro

Chemotherapy-induced nausea and vomiting (CINV) is one of the most common and distressing symptoms occurring in cancer patients. Although the use of serotonin receptor antagonists has greatly improved the CINV control, several patients continue to experience this troublesome side effect. New insights in the comprehension of emesis mechanisms and the discover of the key role of substance P/neurokinin-1 (NK-1) have favoured the development of target inhibitors. Aprepitant blocks NK-1 and has been reported to improve the control of CINV in adults.

A study on the use of aprepitant has been conducted at Humanitas CCO during the last year. A score questionnaire was delivered to patients treated with conventional antiemetic therapy alone or in combination with the new drug. Twenty-two patients received aprepitant: median age was 48 years, M/F ratio 4/18. Fourteen patients were treated with highly emetogenic chemotherapy. Antiemetic therapy was administered by nursing staff and consisted of conventional corticosteroid and anti-serotoninergic treatment plus a capsule of aprepitant 125 mg on day 1 an hour before chemotherapy start, then 80 mg each morning for the next two days.

Aprepitant combined with standard antiemetics moderately improved the control of acute and delayed emesis, compared with standard therapy alone. Five patients reported a mild tiredness during the first two days of treatment.

Aprepitant was effective and safe in our sample of patients, providing an emesis control superior to standard therapy alone.

N33 MANAGEMENT OF CENTRAL VENOUS CATHETERS (CVCS) INFECTIONS PREVENTION: ROLE OF NURSING STAFF

Budelli S., Sedda P., Battisti P., Faedo B., Vozzella A., Di Palma N., Sciarretta C., D'Aprile M., Tomao S.

Onco-Hematology, Santa Maria Goretti Hospital, Latina

The management of CVC such as Port-a-Cath and Groshong is sometimes associated with infections. To prevent these events, nursing and patients education are very important. The aim of this study was to retrospectively analyze the incidence of infections during the management of these devices in our clinical practice.

Methods. In our study, conducted in Onco-hematology Unit of S. Maria Goretti Hospital of Latina, we retrospectively analyzed data of 328 patients with CVCs, 293 with Port-a-Cath (89.3%) and 35 (10.7%) with Groshong. All patients were managed with an aseptic technique during chemotherapy administration, radiological control or heparin treatment. Moreover all patients were instructed for correct domiciliary management of these devices**.** Among 328 patients with CVCs, 218 (66.5%) were admitted in Day Hospital for chemotherapy, while 110 (33.5%) for radiological control or heparin treatment.

Results. No peri-operative infective complications occurred in our patients. Long-term infective complications, defined by the National Nosocomial Infections Surveillance System, appeared in 9 patients (2.7%). Two (0.6%) systemic infections were observed with Groshong. Similarly 7 (2.1%) infective complications were observed with Port-a-Cath: two (0.6%) under skin reservoir outflow, one (0.3%) infectious thrombophlebitis and 4 (1.2%) tunnel inflammations. In all patients at least three blood cultures (one from peripheral blood) were performed, with about 80% of *Staphylococcus aureus* infection diagnosis. In all cases CVC removal and target antibiotic treatment were indicated.

Conclusions. Our findings suggest that although it is generally considered safe, CVCs management can be associated with infective complications. The correct use of national and international guidelines may aid to prevent these events. Thus, an increasing of theoretical knowledge in practice is needed.

N34 THE RELATIONSHIP BETWEEN A WOMAN AFFECTED BY BREAST CANCER AND HER SURGICAL SCAR. WHEN "TOUCHING" BECOMES VERY DIFFICULT. EXPERIENCE FROM A DAY HOSPITAL

Mazzamuto L.[1], Aiello D.[1], La Rocca R.[1], Taibi E.[1], Alì M.[1], Scandurra G.[1], Aiello R.A.[1], Miano E.[1], Caruso M.[1], Caruso F.[2]

[1]UF Oncologia Medica, [2]Direttore Dipartimento Chirurgia Oncologica, Humanitas Centro Catanese di Oncologia, Catania, Italy

Introduction. Despite improvement in oncoplastic and conservative surgery in breast cancer, this kind of interventions highly affects life of women who perceive their body changed, feeling a sense of mutilation and different from the other women and from the past. The woman feels a sense of discomfort with herself and her scar, so that is not able anymore to touch it also affecting the accuracy of follow-up by self-examination.

Surgery should be followed by radiotherapy, endocrine therapy and/or chemotherapy. Patient, ashamed to tell the doctor and not considering suitable the psychologist, often confides to the nurse during the antiblastic therapy.

Our proposal focuses its attention on how she lives the change in her body image and the presence of scars evaluated in cooperation with the psychologist, through the formulation of a questionnaire administered by the nurse.

Materials and method. September 2010-December 2010, 91 women, median age 49 years (range 29-69 yrs), received chemotherapy following quadrantectomy or mastectomy with first-time reconstruction. Fifty-nine patients have consented to receive the test.

Results. 40% of patients showed to have difficulties to carry out self-examination. These were among the younger or women whose physical appearance was particularly important. These started a specific psychotherapeutic "journey" receiving a clinical benefit, a suitable FU, improving social and family life.

The role of the nurse is particularly important because she prepares the patient to receive physical and emotional help and is a medium to the doctor encouraging the patient to see and touch the scar and inviting her to make this journey with the partner.

Conclusions. Accepting the presence of the surgical scar may help the patient accepting, as far as possible, the disease. In our experience nurses, identifying the problem and the psychologist to solve it, are the winning team for the psycho-social rehabilitation of breast cancer patient.

N35 CHEMOTHERAPY RELATED TOXICITIES, QUALITY OF CARE AND ONCOLOGIST-NURSE COOPERATION: THE OP 1 STUDY

Ciancitto R., Russo G., Musumeci L.G., Longhitano M.G., Pulvirenti S., Leonardi C., Scandurra G., Alì M., Aiello R.A., Caruso M.

Department of Medical Oncology, Humanitas Centro Catanese di Oncologia, Catania, Italy

The antineoplastic chemotherapy regimens have side effects standardized according to the NCI-CTC 4.03. This study was aimed to monitor the chemo related toxicities CRT, to train nurses to collect CRT signs and bio-humoral data, also by phone and fax, to establish best supportive care to make more efficient the planning of the chemotherapy restarting. We examined the courses of fifty patients during a period of 1 month. Median age was 56 years (21-73). M/F ratio was 0.19 (8M/42F). The histotypes were: breast 70%, nsc lung 10%, colon 8%, uterine leiomyosarcoma 4%, ovary 2%, pancreas 2%, esophagus 2%, glioblastoma 2%. In breast adjuvant treatment represented 91% of cases with FAC-docetaxel, FEC-docetaxel, AC-docetaxel; first- and second-line represented 6% and 3% of cases with bevacizumab/paclitaxel and trastuzumab/vinorelbine. In non-small cell lung cancer first-line treatment represented 40% of cases with carboplatin/pemetrexed, second- and third-line was 40% and 20% with carboplatin/vinorelbine and gemcitabine. In uterine leiomyosarcoma first-line treatment and third-line represented 50% and 50% of cases with ifosfamide/epidoxorubicin, and pegilated doxorubicin/cyclophosphamide. In ovary first-line treatment represented 100% of cases with carboplatin/paclitaxel. In colonrectum adjuvant treatment represented 34% with De Gramont regimen, first- and fourth-line treatment represented 33% and 33% of cases with capecitabine. In pancreas first-line treatment represented 100% of cases with gemcitabine/oxaliplatin. In esophagus chemoradiation represented 100% with cisplatin regimen. In glioblastoma the adjuvant treatment represented 100% of cases with temozolamide. Neutropenia was G1 in 8% of cases, G3 in 6%. Anemia was G1 in 56%, G2 in 6%. Thrombocytopenia was G1 in 6%, G2 in 2%. Stomatitis was G1 in 12%, G2 in 6%. Diarrhoea was G1 in 6%, G2 in 2%. Emesis was G1 in 24%, G2 in 12%. Nurse monitoring CRT increased perceived quality of care, made it possible a faster planning and a reduction of unnecessary access to our department, so we recommend this approach.

N36 NURSING PRACTICE TO PREVENT INFECTION IN HOSPITALIZED NEUTROPENIC PATIENTS

Stabile C., Oliveri A., Vignera C., Vinciguerra A., Sciacca I., Cucchiara F., Anfuso R., Boland D., Nicotra C., Reale S., Chiarenza M., Mazzola A., Caruso M.

Humanitas Centro Catanese di Oncologia (CCO), Department of Medical Oncology, Catania, Italy

Neutropenia is reduced neutrophil white blood cell count frequently related to cytotoxic chemotherapy or wide bone irradiation. Patients with severe neutropenia have an increased risk of infections and require a strict isolation. Few studies have demonstrated the efficacy of low microbial food and water, protective environments and clothing or special skin antisepsis in reducing the risk of infections. Nevertheless, some of these practices seem prudent and reasonable.

The primary objective of nurse care is to create a safe and peaceful environment that assures a good quality of life to the immunosuppressed patient. Simultaneously, the infection control practitioner should assist the nurse in understanding what an immunosuppressed patient is, what his risk of infection is, what his reaction to infection might be, and what isolation practices are appropriate.

The nurse must use the principles of asepsis in all patient care activities, recognize risk factors of infection, and understand the importance of procedures such as proper nutrition, oral hygiene, and skin cleaning. A careful nursing intervention may be helpful in controlling or preventing healthcare-associated infections in neutropenic patients. Therefore, our institution has adopted detailed nursing guidelines for managing all patients with severe neutropenia.

AUTHOR INDEX

See you at the

14th National Congress of Medical Oncology
Roma (Italy), 27-29 October, 2012

President of the Congress
Marco Venturini

Scientific Secretariat
Aiom

Via Enrico Nöe, 23
20133 Milan, Italy
Phone: +39.02.70630279
Fax: +39.02.2360018
aiom@aiom.it
www.aiom.it

Organizing Secretariat
Aiom Servizi s.r.l.

Milan Office
Via Enrico Nöe, 23
20133 Milan, Italy
Phone: +39.02.26683129
Fax: +39.02.59610555
info@aiomservizi.it

Rome Office
Via Domenico Cimarosa, 18
00198 Rome, Italy
Phone: +39.06.8553259
Fax: +39.06.8553221
info@aiomservizi.it