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gastrointestinal tumors

709PD FIVE-YEAR RESULTS OF THE RANDOMIZED PHASE III TRIAL COMPARING S-1 MONOTHERAPY VERSUS SURGERY ALONE FOR STAGE II/III GASTRIC CANCER PATIENTS AFTER CURATIVE D2 GASTRECTOMY (ACTS-GC STUDY)

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Background: The results of the first interim analysis of the ACTS-GC study was reported in ASCO-GI meeing in 2007 and published soon after (Sakuramoto S et al. N Engl J Med 2007; 357:1810-20), as they showed significant survival benefit of S-1 monotherapy for stage II/III gastric cancer patients after D2 surgery. As 5 years have passed after completion of the enrollment, originally planned analysis was carried out using up-dated survival data to confirm the results and conclusion drawn from the interim analysis.

Method: Eligibility included R0 resection, pathological stage II/III (Japanese Classification, version 2), age ranged 20-80, no prior adjuvant treatment, adequate organ function. Pts were randomized to S-1 (80-120mg/day according to the body surface, 4 weeks administration with 2 weeks off in each course, starting within 45 days of surgery till 1 year after surgery,) or surgery alone (C). Primary end point was overall survival (OS). Assuming 500 pts in each, the study had 80% power to detect 0.70 HR for S-1 to C in OS at 0.05 two-sided alpha.

Results: Between 10/2001 and 12/2004, 1059 pts were randomized (529 to S-1 and 530 to C). 25 pts were ineligible. There was no background difference between the groups. 474, 409, 175 pts were stage II, IIIA, IIIB respectively. 943(89%) pts could be followed up more than 5 years after surgery. Median follow-up time was 5.46 years. 139 and 196 pts have died in S-1 and C group, respectively. HR for death in S-1 to C was 0.65 (95%CI, 0.53-0.81). OS at 5-years for all randomized pts was 72.6% (95% CI, 68.7-76.5%) for S-1 and 61.4% (57.2-65.7%) for C. HR of stage II, IIIA, and IIIB was 0.48, 0.69 and 0.79 respectively. 5-year OS of each stage in S-1 group was 85%, 68% and 51%, respectively.

Conclusion: We could confirm with up-dated survival data that adjuvant chemotherapy with S-1 for gastric cancer is feasible and highly effective, if patients undergo D2 surgery.

Disclosure: All authors have declared no conflicts of interest.

710PD SORAFENIB DOES NOT IMPROVE THE RESULTS OF CHEMOTHERAPY IN ADVANCED PANCREATIC CANCER: A GISCAD RANDOMISED PHASE II TRIAL

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Background: No standard treatment is available for advanced pancreatic cancer (PC).Although gemcitabine (GEM) is used with the purpose of symptom palliation,there is no clear evidence of a significant survival increase.Attempts at improving results by combining GEM with other cytotoxic drugs failed to obtain any advantage.KRAS and BRAF mutations are present in approximately 90% and 5% of the PCs,respectively.Sorafenib is an inhibitor of the RAS/RAF signalling pathway showing inhibition of proliferation of pancreatic tumour cell lines containing KRAS or BRAF mutations.It may be combined with gemcitabine and cisplatin without any pharmacokinetic interaction or enhanced toxicity.Therefore,a phase II randomised trial was designed to explore the role of sorafenib in combination with chemotherapy (CT).

Methods: Patients with histologically proven,locally advanced or metastatic PC,chemonaive and ECOG 0-2 were eligible.Subjects were randomized to receive cisplatin 25 mg/m^2/day and GEM 1000 mg/m^2/day on d1-8q21days plus Sorafenib,at 400 mg (2 tabletsx200 mg each) orally,twice daily continuously (arm A),or GEM/cisplatin alone (arm B).The primary end point was Progression Free Survival (PFS),other end points were response rate (RR) and overall survival.

Results: 114 patients were enrolled.Patients characteristics are summarized in the table.

Characteristics	Sorafenib/CT (58)	CT (56)
M/F	36/22	30/26
Median age(yrs)	66.6	65.1
Locally advanced	16	22
Metastatic	42	34
ECOG 0-1	40	40

At a median follow up of 13.4 months,39 patients progressed in arm A and 40 in arm B.Median PFS was 4.5 months and 3.3 months respectively (HR=1.01;0.68–1.55 CI 95%).Objective RR was 6.9% in arm A and 7.1% in arm B.Rate of responders/stable disease was 58.6% in arm A and 53.6% in arm B (P=0.47).Haematological and hepatic toxicity was the cause of discontinuation in 6 (10.3%) patients in arm A and 5 (8.9%) in arm B.

Conclusions: Addition of sorafenib to CT does not seem to significantly improve PFS and RR in advanced PC.The analysis of the molecular alterations of the RAS/RAF pathway is ongoing.

Disclosure: All authors have declared no conflicts of interest.

711PD IMPACT OF CIRCUMFERENTIAL MARGIN (CRM) SIZE ON OVERALL SURVIVAL (OS) IN OESOPHAGEAL CANCER (OC)

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Background: We investigated the prognostic value of the size of the CRM on overall survival (OS) and the impact of post-op chemoradiation (CRT) as salvage therapy for patients with positive CRM.

Methods: From Jan 2000 - June 2007 patients (pts) undergoing oesophageal resection were collected on a prospective database. All surgery (S) was performed by 2 specialist surgeons at a single centre. Pts with OC and type 1 GOJ tumours on final pathology were included. TNM stage, histological type, grade, site, operation performed, neoadjuvant and adjuvant treatment details were extracted retrospectively. Exact CRM size in mm was obtained from pathology reports or original slides. Pts with +ve longitudinal resection margin (LRM) were excluded. Recurrence and OS data were collected up to July 2009 or to a minimum of 5 years after S. Dates and details of 1st recurrence were collected from restaging scans. Date of death was obtained from the cancer registry.

Results: 229 pts were included, 6 excluded for +ve LRM and 5 as exact margin size details were not available. CRM size was grouped into 0mm (45pts), less than 1mm (48 pts), 1-1.9mm (31 pts), greater than/equal to 2mm (105 pts). Median followup 32.5 months. There were 125 deaths. Median OS 3.3 years (95% CI 2.8-6.2). Median OS by CRM: 0mm 1.2yrs (95% CI 0.9-1.4), less than 1mm 1.9yrs (95% CI 1.4-3.2), 1-1.9mm 3.5yrs (95% CI 2-no upper CI), greater than 2mm not reached. P-value for log rank test comparing all 4 groups: 0.0001. 61 pts with CRM of 0 or less than 1 mm with postop CRT were compared with 32 without. The median OS for the 2 groups were not different (1.3 vs 1.3 years, p-value for log rank test comparing the 2 groups: 0.786). A Cox regression analysis was performed confirming the independent prognostic value of CRM size (OR 3.26). No CRM size was found beyond which there was no further increase in OS.

Conclusion: CRM size is a significant prognostic factor for OS in OC with no clear cut-off that can be recommended as an optimum CRM. In pts with CRM of 0 or less than 1mm, postop CRT did not alter OS.

Disclosure: All authors have declared no conflicts of interest.

712PD **RANDOMIZED PHASE II TRIAL WITH AN UPA INHIBITOR (WX-671) IN PATIENTS WITH LOCALLY ADVANCED NON-METASTATIC PANCREATIC CANCER**

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Background: WX-671 (Mesupron) is an orally available prodrug of WX-UK1, a serine protease inhibitor that inhibits uPA as well as other serine proteases. WX-UK1 (Setyono-Han et al., Thromb Haemost 2005) and WX-671 have shown to efficiently reduce primary tumor growth and metastasis formation in a variety of animal models. The proteolytic factor uPA and its inhibitor PAI-1 belong to those biological factors which have provided the highest level of evidence (LOE1) in terms of their prognostic and predictive significance. WX-671 is currently the only drug in Phase II aiming at this target.

Methods: 95 patients with locally advanced, non-resectable, non metastatic pancreatic cancer were randomized to three cohorts receiving daily oral WX-671 as hydrogen sulfate corresponding to 200 and 400 mg WX-671 free base or no WX-671. In addition, all patients were treated with weekly gemcitabine (1000 mg/m^2 i.v. as per SPC). Treatment continued until disease progression or toxicity. Safety was assessed by measuring vital signs, laboratory parameters (hematology, blood chemistry, coagulation) and ECGs. Efficacy endpoints were response rate at the various staging intervals, progression free survival, time to first metastasis, overall survival as well as changes in tumor- and uPA-system-related markers.

Results: All 95 patients were accrued between Jun 2007 and Aug 2008. Efficacy was assessed by a central reader at regular intervals based on digital CT images. Data collection has been closed in Jan 2010. Response rate of the combination was 12.9 % compared to 3.8% for Gemcitabine alone. 1-year PFS rate was increased from 16.2% (gemcitabine alone) to 26.9% for the combination of gemcitabine with 400 mg WX-671. Overall survival showed an increase from 9.9 mo (gemcitabine alone) to 12.5 mo for the combination of gemcitabine and WX-671. 1-year survival increased from 33.9% with gemcitabine to 50.6% for the combination.

Conclusions: The combination of daily oral WX-671 in combination with weekly i.v. gemcitabine was well tolerated and demonstrated anti-tumor activity which led to promising increase in overall survival.

Disclosure: C. Mala: Wilex AG, Director Clinical Research; N. Neville: Wilex AG, Vice President CR+D. P. Bevan: Wilex AG, Director. All other authors have declared no conflicts of interest.

713P **RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTRE PHASE III STUDY OF CAPECITABINE / CISPLATIN + BEVACIZUMAB (BEV) OR PLACEBO (PL) AS 1ST-LINE THERAPY IN PATIENTS (PTS) WITH ADVANCED GASTRIC CANCER (AGC) (AVAGAST UPDATE)**

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Background: Median survival for pts with inoperable AGC in most phase III studies is <1 year. The addition of bev to chemotherapy (chemo) is supported by a strong preclinical rationale and phase II evaluation. AVAGAST compared the efficacy/safety of bev + chemo vs pl + chemo.

Methods: Pts with inoperable, locally advanced/metastatic stomach/gastroesophageal junction adenocarcinoma with no prior therapy were randomized 1:1 to capecitabine (cape, or 5-FU) + cisplatin (cis) and either bev (7.5 mg/kg iv) or pl q3w. Stratification variables: geographical region, fluoropyrimidine treatment, disease status. Cis was given for 6 cycles and bev/pl + cape/5-FU until disease progression or unmanageable toxicity. Primary objective: overall survival (OS); secondary objectives: progression-free survival (PFS), overall response rate (ORR), safety (assessed by independent DSMB), quality of life, biomarkers.

Results: 774 pts were enrolled from Sep07 to Dec08. Treatment arms were balanced for stratification variables with the exception of advanced disease (2% vs 5%). Approx 95% of pts were metastatic, two-thirds male, 49% from Asia/Pacific, 32% from Europe and 19% from the Americas. Median OS was 10.1 mo with chemo + pl and 12.1 mo with chemo + bev (table). While the primary endpoint was not met, median OS and PFS were different across regions (table). Safety analyses did not reveal any new findings and an acceptable safety profile was found for chemo + bev (table).

	Chemo + pl (n=387)	Chemo + bev (n=387)	p-value	HR (95% CI)
Efficacy – ITT Median OS, mo Median PFS, mo ORR, %	10.1 5.3 29.5	12.1 6.7 38.0	0.1002 0.0037 0.0121	0.87 0.80 –
Median OS by region Americas, mo Europe, mo Asia Pacific, mo	6.8 8.6 12.1	11.5 11.1 13.9	– – –	0.63 (0.43–0.94) 0.85 (0.63–1.14) 0.97 (0.75–1.25)
Median PFS by region Americas, mo Europe, mo Asia Pacific, mo	4.4 4.4 5.6	5.9 6.9 6.7	– – –	0.65 (0.46–0.93) 0.71 (0.54–0.93) 0.92 (0.74–1.14)
Safety events of special interest (G3–5), % Hypertension Haemorrhage Wound-healing complications GI perforation ATEs VTEs 60-day mortality	0.5 3.9 0.0 0.3 2.1 9.4 5.8	6.2 3.9 0.5 2.3 1.3 6.5 3.1		

Conclusion: In the entire study population, OS was not improved with the addition of bev, although there were significant improvements in PFS and ORR. Regional differences in efficacy are noted, and further subgroup analysis is ongoing, including biomarker analysis, in order to understand the potential role of bev in AGC.

Disclosure: E. van Cutsem: Member on Advisory board: Roche Corporate-sponsored research with Roche; M. Shah: Corporate-sponsored research with Genentech; Y. Kang: Member on Advisory board: Roche Honoraria from Roche; J. Wu: Employed by Roche; B. Langer: Employed by Roche. All other authors have declared no conflicts of interest.

714P **NOVEL CHEMOTHERAPY COMBINATIONS IN ADVANCED GASTRIC CANCER: AN UPDATED META-ANALYSIS**

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Combination chemotherapy is widely accepted for patients with advanced gastric cancer, but uncertainty remains regarding the choice of the regimen.

Objectives: To assess the effect of: Comparison 1) irinotecan versus non-irinotecan-containing regimens, comparison 2) docetaxel versus non-docetaxel-containing regimens, comparison 3) regimens including oral 5-FU prodrugs versus intravenous fluoropyrimidines, comparison 4) oxaliplatin versus cisplatin-containing regimens on overall survival.

Search Strategy: We searched: Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, proceedings from ECCO, ESMO, ASCO until December 2009.

Selection Criteria: Randomised controlled trials on the above mentioned chemotherapy regimens in advanced or metastatic adenocarcinoma of the stomach or GE-junction.

Results: The meta-analysis of overall survival for comparison 1) included 4 trials, 640 patients, and results in a HR of 0.86 (95% CI 0.73-1.02) in favour of the irinotecan-containing regimens. For comparison 2) 4 trials with a total of 924 patients have been included in the analysis of overall survival. The resulting HR is 0.93 (95% CI 0.79-1.09) in favour of the docetaxel-containing regimens, with moderate heterogeneity (I^2 =7%). For comparison 3 and 4, one major relevant study (Cunningham 2008) could not be included in this meta-analysis after discussion because it included patients with squamous cell cancer of the esophagus as well. Thus, for comparison 3) one relevant study (Kang 2009; 316 patients) comparing capecitabine versus 5-FU in combination with cisplatin is eligible. The resulting HR is 0.85 (95%CI 0.65-1.11) in favour of the oral regimen. For comparison 4) two eligible trials were identified (Al Batran 2008, Popov 2008; 292 patients) with a resulting HR of 0.82 (95% CI 0.47-1.45) in favour of the oxaliplatin-based regimens. For three further trials data is incomplete at present.

Conclusions: Chemotherapy combinations including irinotecan, oxaliplatin, docetaxel or oral 5-FU prodrugs are alternative treatment options to cisplatin/5-FU or cisplatin/5-FU/anthracycline-combinations, but do not provide significant advantages in overall survival. Supported by: KKS Halle, grant number [BMBF/FKZ 01GH01GH0105].

Disclosure: All authors have declared no conflicts of interest.

715P EPIRUBICIN (E) IN COMBINATION WITH CISPLATIN (CDDP) AND CAPECITABINE (C) VERSUS DOCETAXEL (D) COMBINED WITH 5-FLUOROURACIL (5-FU) BY CONTINUOUS INFUSION (C.I.) AS FRONT-LINE THERAPY IN PATIENTS WITH ADVANCED GASTRIC CANCER (AGC): PRELIMINARY RESULTS OF A RANDOMISED PHASE II TRIAL OF THE GRUPPO ONCOLOGICO DELL'ITALIA MERIDIONALE

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Background: Results of randomized phase III trials support the use of systemic chemotherapy as palliative treatment of patients with AGC with remission rates of 40%–60% and median survival times of 8–11 months. However, there is no globally accepted standard regimen for the first-line treatment of advanced disease. Compared with ECF, D in combination with 5-FU c.i. has shown a very interesting activity in a phase II randomised study (J Clin Oncol 23: 494; 2005). REAL-2 trial demonstrated that C was effective as 5-FU c.i. when used as part of a triple combination regimen turning the treatment into an easier to administer regimen (N Engl J Med 358: 36; 2008). In the present study we evaluated in a phase II non-comparative trial the activity of DF and ECX as first-line therapy of AGC.

Patients and methods: Patients with previously untreated histologically documented AGC, with at least one measurable disease, age < 18 years, ECOG PS ≤ 2, and age 18-75 years, were randomly assigned to receive E (50 mg/m^2 day 1), CDDP (60 mg/m^2 day 1) and C (625 mg/m^2 bid, days 1-21) (ECX) or D (85 mg/m^2 day 1) and 5-FU (750 mg/m^2/day c.i., days 1-5) (DF) q 3 weeks. RECIST and NCI criteria were employed to determine the activity and the toxicity of these regimens.

Results: The main characteristics in ECX and DF arms were: M/F = 22/14 and 23/8, median age = 58 years (range 39-74 years) and 61 years (range 44-75 years), site of disease = liver in 29 (82.8%) and in 20 (64.5%) patients, lung in 7 (20%) and in 4 (12.9%) patients, lymph-nodes in 26 (74.2%) and in 21 (67.7%) patients, multiple 14 (20%) versus 21 (60%) and 16 (51.6%) versus 14 (48.4%). ORR (CR + PR) was 54.3% in ECX arm and 22.6% in DF arm. Nine PRO were observed in both arms (25.7% and 29.2%, respectively). Main toxicity rate (G3-4) in the evaluable patients assigned to ECX arm were neutropenia (28.5% versus 19.4%), nausea/vomiting (18.2% versus 3.2%), alopecia (22.8% versus 18.3%) and HandF syndrome (5.7% versus 0%). The worst toxicity (G3-4) in DF arm was anaemia (9.6% versus 5.7%).

Conclusions: Our preliminary data suggest an higher ORR for ECX regimen when compared to DF with a favourable toxicity profile. Definitive data will be presented during the meeting.

Disclosure: All authors have declared no conflicts of interest.

716P MFOLFOX-4 FOLLOWED BY MFOLFIRI OR THE REVERSE SEQUENCE IN METASTATIC GASTRIC CANCER

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Background: Both FOLFOX and FOLFIRI regimen have been evaluated in a number of phase II studies in the first- and second-line treatment of metastatic gastric cancer. This study investigated two sequences: low dose leucovorin (ldLV), 5-FU, and oxaliplatin (modified FOLFOX-4) followed by ldLV, 5-FU, and irinotecan (modified FOLFIRI; arm A), and mFOLFIRI folllowed by mFOLFOX (arm B).

Patients and methods: Previously untreated patients with metastatic or recurrent gastric cancer were received leucovorin 20 mg/m2 iv bolus followed by a 5-FU iv bolus 400mg/m2 and 22-hour continuous infusion 600mg/m2 on day 1 and 2, either with oxaliplatin 85mg/m2 or with irinotecan 150mg/m2 on day 1 every 2 weeks. At progression, oxaliplatin was replaced by irinotecan, or irinotecan by oxaliplatin.

Results: Median survival was 11.3 months in 40 patients treated by mFOLFOX4 then mFOLFIRI versus 9.7 months in 37 patients treated by mFOLFIRI then mFOLFOX-4 (p = 0.143). Median second time to progression (TTP) was 6.4 months in arm A versus 5.7 months in arm B (p = 0.015). In first-line therapy, mFOLFOX-4 achieved 37.5% response rate (RR) and 2.9 months median TTP, versus mFOLFIRI which achieved 27% RR and 2.9 months TTP (p = 0.154). Second-line mFOLFOX-4 achieved 10.8% RR and 1.7 months TTP, versus mFOLFIRI which achieved 15.4% RR and 2.2 months TTP (p = 0.036).

Conclusion: Both sequences achieved a similar efficacy in overall survival, but mFOLFOX-4 followed by mFOLFIRI was slightly preferred in time to progression.

Disclosure: All authors have declared no conflicts of interest.

717P AN INTERIM ANALYSIS OF A PHASE II, OPEN-LABLE, MULTI-CENTER, PROSPECTIVE STUDY OF PACLITAXEL PLUS CAPECITABINE WITH SUBSEQUENT CAPECITABINE MAINTENANCE AS FIRST-LINE TREATMENT IN ADVANCED GASTRIC CANCER

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Background: Small sample studies have shown the efficacy and safety of paclitaxel in advanced gastric cancer(AGC). However, the role of paclitaxel in the chemotherapy of AGC needs to be confirmed by large scale study. So in this open label, phase II, multi-center prospective study(ML20312), we observed the efficacy and safety of paclitaxel plus capecitabine with subsequent capecitabine as first-line treatment for AGC.

Methods: Patients with previously untreated metastatic gastric adenocarcinoma, signed informed consent, evaluable lesion(s) by RECIST, KPS≥70 and adequate organ functions are eligible. Paclitaxel is given with 80mg/m^2 for 3-hour infusion on day 1,8, capecitabine is given with1000 mg/m^2 twice daily day 1-14 (PX, every 3weeks) until progression or maximum 6 cycles or unendurable adverse events(AEs) or withdraw consent. Subsequently, the patients with no progression were given maintenance therapy of capecitabine monotherapy (X) with same dose/schedule as the combination therapy until progression or unendurable AE or withdraw consent. Progression free survival(PFS) is the primary endpoint, objective response rate (RR), disease control rate(DCR), overall survival (OS) and safety are the second end points.

Results: From Dec 2006 up to now, 194 patients(128 men, 66women) were enrolled in 21 centers, 185 patients had been followed up more than 3 months. The median age was 59 years (range 23 - 80). Median treatment duration was 5 cycles. Tumor response was evaluated in 165 cases, CR and PR were achieved in 1.2% (2 cases) and 38.2% (63 cases) of patients (RR 39.4%), 75 patients had stable disease (45.5%), and 25 patients (15.1%) progressed. The disease control rate was 84.9%. After median follow-up of 11.6 months, 119 cases progressed and 87cases died. Inmature data shows estimated PFS of 206 days (95%CI:167.8-244.2). Grade3/4 toxicities were leucopenia (14.6%) and neutropenia (8.6%), alopecia(14.1%), fatigue(7.0%)ï¼Œnausea/vomiting(5.4%), hand-food syndrome(5.4%), diarrhea(3.8%), neurotoxicity(3.2%), hepatic disfuction(2.7%). No treatment-related deaths were recorded in all patients.

Conclusion: PX-X as first-line treatment was promising in AGC. Based on the preliminary data of the phase II study, the phase III study (ML22697) has been launched for further investigation.

Disclosure: All authors have declared no conflicts of interest.

718P BIWEEKLY DOCETAXEL, FLUOROURACIL, LEUCOVORIN, OXALIPLATIN (TFOX) FOR ADVANCED GASTRIC AND OESOPHAGEAL ADENOCARCINOMA (AGEC): TOLERANCE AND RESPONSE IN 38 PATIENTS: PRELIMINARY REPORT

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Introduction/Objectives: The Docetaxel-Cisplatin-5FU association is superior to 5FU-Cisplatin in term of response rate (RR) and overall survival (OS) in advanced gastric cancers, but is more toxic. We hypothesize that incorporating Docetaxel into a simplified FOLFOX regimen should be a tolerable and efficient option in AGEC.

Aims and Methods: The biweekly intravenous TFOX combines Docetaxel (50mg/m2), oxaliplatin (85mg/m2) on day 1, and 5FU continuous infusion for 48h (2400mg/m2) administered every 2 weeks. Population: 38 patients (pts) with AGEC; 29 with gastric (6 linitis plastica) and 9 oesophageal adenocarcinoma, locally advanced (n=17/38) or metastatic, (21/38); 31/38 pts were PS 0 or 1; median age was 60 years (38-73); TFOX was administered as first line in 16 pts, in 2-3rd line in 22 pts. Efficacy evaluation was made every 3 or 4 cycles according to the RECIST criteria.

Results: Mean number of cycles: 5,5 cycles (1-24), and 86% of pts received at least 4 cycles; 3 pts have received only 1 or 2 cycles and not evaluated. Responses were evaluable in 32 pts; Overall Response Rate: 65,6% (n=21), Complete response (CR) in 4 pts (12,5%), partial response (PR) in 53,1%; RR: 71,4% with 14,3% CR in 14 locally advanced cancer, 61,1% with 11% CR in 18 metastatic AGEC, and 100% in 4 linitis plastica with 1 CR. Median PFS: 5,7 months (95%CI: 3,9-10,3); Median OS: 11,2 months (95%CI: 5,1-23,1).

Complementary treatments were facilitated in 17 pts (association of chemo-radiotherapy in 7 pts and surgical excision in 10 with 6 R0 resection in 3 metastatic, 3

locally advanced and 3 R1 resection). Two pts with peritonal carcinomatosis had a CR after TFOX and received intraperitoneal chemohypertherma.

Tolerance of TFOX was good with no treatment-related deaths and 1 patient (3%) having a febrile neutropenia. The most frequent NCI-CTC grade 3 or 4 non-hematolological toxic effects was periperal neuropathy (19%) and diarrhea (10%).

Conclusion: These results showed that TFOX is effective and tolerable in AGEC, it may facilitate secondary resection in initially non resectable cancer and should be evaluated in randomized trials.

Disclosure: All authors have declared no conflicts of interest.

719P PHASE II STUDY OF WEEKLY PACLITAXEL, CISPLATIN, AND 5-FLUOROURACIL (PCF) FOR ADVANCED GASTRIC CANCER

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Background: Our previous phase I study (Cancer Chemother Pharmacol. 2007, 59:631-6) provided evidence that combination chemotherapy with paclitaxel, cisplatin, and 5-fluorouracil (PCF) is effective and well tolerated in patients with advanced gastric cancer (AGC). Characteristics of this weekly regimen are its ability to be performed on an outpatient basis and its indication for patients unable to tolerate oral intake. This phase II trial was conducted to confirm the efficacy and toxicity of PCF.

Methods: Eligibility criteria were as follows: pathologically confirmed gastric carcinoma, measurable lesion, absence of any history of treatment with taxanes, platinum-based compounds, or 5-fluorouracil (one regimen of pretreatment with oral 5-fluorouracil agents was allowed), age > 20, ECOG PS 0-2, adequate organ function, and written informed consent. Paclitaxel (80 mg/m2), cisplatin (25 mg/m2), and 5-fluorouracil (600 mg/m2, bolus) were administered on days 1, 8, and 15, repeated every four weeks. The primary endpoint was objective response evaluated by RECIST guidelines, secondary endpoints were overall survival, progression-free survival and safety.

Results: 46 patients were enrolled. 45 patients were assessable for efficacy and safety. Patient characteristics: male/female = 36/10; median age 71 (range 48-85); PS 0/1 = 18/28. Seventeen had a history of pretreatment with oral 5-fluorouracil agents (16 received S-1 and 1 received 5'DFUR). Median cycles 4.5 (range: 1-24). Response rate (CR+PR) was 55.5% (95%CI: 41.0-70.0) with 2 patients showing complete response. Disease control rate (CR+PR+SD) was 82.2% (95%CI: 71.1-93.4). Median progression free survival was 160 days (95%CI: 145-214). Median overall survival was 552 days (95%CI: 350-843). Grade 3-4 major adverse reactions were neutropenia (75.6%), leucopenia (37.8%), anemia (26.7%), febrile neutropenia (22.2%), exacerbation of PS (15.6%), and anorexia (13.3%). There were no treatment-related deaths.

Conclusions: The PCF regimen was well-tolerated and showed promising activity for AGC. In addition, attention was focused on achieving a comparable response in patients with a history of being treated with an oral 5-fluorouracil agent.

Disclosure: All authors have declared no conflicts of interest.

720P RETROSPECTIVE STUDY REGARDING THE EFFICACY OF 2ND OR HIGHER LINE CHEMOTHERAPY OF PATIENTS IN ADVANCED OR RECURRENT GASTRIC CANCER (ARGC) AFTER THE FAILURE OF S-1 OR S-1 COMBINATION CHEMOTHERAPY (S+α)

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Background: At the 2007 ASCO annual meeting, the JCOG 9912 and the SPIRITS trial showed that S-1 (S) and CDDP/S-1 (S+P) therapy to now are an accepted standard chemotherapeutic regimens for advanced and recurrent gastric cancer (ARGC). Today in Japan, S+α are the mainstay treatments for ARGC. However, it is important to acquire a longer survival for ARGC and therefore development of a 2nd line or higher chemotherapy after S+α treatment failure is thus required. The present study set out to identify the factors which make it appropriate to perform the chemotherapy after S+α failure, and to examine the validity of this treatment.

Methods: Forty-two patients with ARGC who failed to sufficiently respond to S+α treatment between December 2004 and May 2009 were retrospectively reviewed.

Results: The patient characteristics were as follows: mean age, 64.4 years of age; sex, M/F=29/13; patient status: unresectable:23, non-curative operation:13 and postoperative recurrence: 6. The initial treatment regimens consisted of S:25,S+P:16, DTX+S:1. The MST since the S+α administration was 699 days. The median TTF of S+α therapy was 137 days. The 2nd-line treatment regimens included Taxanes:30, CPT-11:11,S+P:1. The median number of 2nd or more treatment courses was 2 (1-5). The RR of 2nd line therapy was 14% (PR6, SD29, PD7). The median TTF and OS since the 2nd-line chemotherapy was administered were 231 days and 345 days, respectively. The median TTF of 2nd-line chemotherapy alone was 112 days, while the median TTF of the 3rd line therapy (or more) was 231 days. The OS since the time of the S+α administration significantly correlated with the TTF of S-1+α($p<0.0063$), while the OS since the 2nd-line treatment administration (2nd OS) was independent of the TTF of S+α. The 2nd OS did not correlate with either the specific type of 2nd-line regimens or the total number of regimens the patients received.

Conclusions: The findings of this study suggest that the addition of a 2nd line chemotherapy (or more) is expected to result in a longer survival for patients with ARGC, even when the anti-tumor effect was deemed to be insufficient following the S+α treatment.

Disclosure: All authors have declared no conflicts of interest.

721P TRIPLET COMBINATION OF CAPECITABINE PLUS OXALIPLATIN AND IRINOTECAN IN THE TREATMENT OF PATIENTS WITH PREVIOUSLY UNTREATED ADVANCED GASTRIC CANCER (AGC)

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Purpose: The three-drug regimen including capecitabine, oxaliplatin and irinotecan (COI) is an effective and well-tolerated upfront treatment for advanced colorectal cancer (Ann Oncol 2007; 18:1810-16). Because this regimen contains some newer cytotoxic agents commonly used in the palliative treatment of AGC, we investigated the activity and safety of this combination regimen against gastric cancer.

Methods: COI (capecitabine 1000 mg/m^2 PO twice daily on days 2 to 6; oxaliplatin 85 mg/m^2 IV on day 2; and irinotecan 180 mg/m^2 IV on day 1 of a biweekly schedule) was administered to patients who had advanced or metastatic disease, aged £75 years, and an ECOG performance status of 0-1 either until they had evidence of progressive disease or for a maximum of 8 cycles. Objective responses (RECIST criteria) were assessed every 4 cycles.

Results: Forty-one consecutive patients (26 males and 15 females) who had a median age of 60 years (range, 41-74 years) were enrolled to receive the COI regimen. Six patients (14%) had locally advanced disease, and 16 patients (39%) retained the primary gastric lesion. Main disease sites included lymph nodes (43%), peritoneum (34%), and liver (24%). At present, 36 patients are assessable for response and toxicity. Five patients are still receiving chemotherapy before follow-up response assessment. A complete response was observed in 5 patients, and a partial response in 9 patients (ORR 38.9%; 95% CI, 23.1-56.5%). Stable disease occurred in 13 patients (36%). Analysis of both median time to progression and survival is still pending. Evaluable patients were treated with a median of six cycles (range, one to 8 cycles). The most common severe toxicities were grade 3 diarrhea and nausea that occurred in 32% and 25% of patients, respectively.

Conclusions: These preliminary data show that the COI regimen has activity as upfront therapy in fit patients with AGC, and it has a manageable toxicity. The ease of administration and good safety profile can make the COI regimen well suited for use as a platform for newer combinations with other biologic agents. (The authors would like to thank the I.T.M.O. service for data analysis).

Disclosure: All authors have declared no conflicts of interest.

722P SURVIVAL BENEFIT ASSOCIATED WITH FLUOROPYRIMIDINES, PLATINUM AGENTS, TAXANES, AND IRINOTECAN DURING ALL LINES OF TREATMENT IN PATIENTS WITH ADVANCED GASTRIC CANCER

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Background: Several agents were approved for AGC in Japan around 2000 (irinotecan in 1994, S-1 in 1999, docetaxel in 2000, and paclitaxel in 2001). However, the impact of the exposure to several cytotoxic agents during all lines of treatment on overall survival (OS) of patients with AGC has not yet been evaluated in detail as colorectal cancer.

Methods: We conducted the retrospective analysis of 704 patients with AGC who underwent chemotherapy in our institution to evaluate the impact of exposure to different agent classes on OS using the novel time-varying covariate (TVC) analysis.

Results: Median OS was 12.3 months. The frequency of exposure to each agent class during all lines of treatment was 92.6% for FU (5-fluoroiracil or oral

fluoropyrimidine), 48.2% for platinum agents, 65.1% for taxanes, and 39.1% for irinotecan. According to a multivariate Cox model with exposure to each agent class as a time-varying covariate, the hazard ratios (HR) of death were 0.41 (95% CI, 0.27-0.57; p<0.001) for FU, 0.71 (95% CI, 0.58-0.84; p<0.001) for platinum agents, 0.51 (95% CI, 0.41-0.63; p<0.001) for taxanes, and 0.53 (95% CI, 0.43-0.65; p<0.001) for irinotecan. Although other agents were used in 18.6% of patients, they did not impact survival.

Conclusions: Each of the four agent classes (FU, platinum agents, taxanes, and irinotecan) appear to be independently associated with improved OS in patients with AGC. This result suggests the importance of a strategy to make these active agents available to all patients with AGC to prolong OS.

Disclosure: All authors have declared no conflicts of interest.

723P PHASE 2 STUDY OF TELATINIB IN COMBINATION WITH CAPECITABINE AND CISPLATIN AS FIRST-LINE TREATMENT IN PATIENTS WITH ADVANCED CANCER OF THE STOMACH OR GASTRO-ESOPHAGEAL JUNCTION (GEJ)

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Telatinib (tel) is a highly selective and potent oral kinase inhibitor with activity against VEGFR1-3, PDGFR, and KIT tyrosine kinases. Phase 1 studies demonstrated that twice daily (bid) administration of tel up to 1,500 mg is well tolerated using a continuous dosing regimen. Disease control rate (DRC) was 50% (> 3 months), with partial responses (PR) in renal cancer patients. 900 mg bid dose was recommended for Phase 2.

Design: TEL0805 is a multicenter Phase 2 study assessing tel in combination with capecitabine (X) and cisplatin (P) in previously untreated metastatic or unresectable gastric or GEJ adenocarcinoma patients. Tel was administered at 900 mg bid continuously in combination with X 1,000 mg/m^2 bid on days 1-14 of a 21-day cycle. P was administered 80 mg/m^2 on day 1 of the first six cycles. The primary efficacy endpoint was progression free survival (PFS). Treatment was continued until disease progression or unacceptable toxicity.

Results: 34 pts were enrolled (16 gastric, 18 GEJ; 33 stage IV/1 stage III) and 28 were evaluable for response at 42 days. The overall response rate (ORR) was 64% (1 complete response (CR), 17 PR). An additional 8 patients had stable disease (SD), for an overall DCR of 93%. Median PFS has not been achieved with a median follow up 90 days (range 43 to 214 days). Common grade 3/4 adverse events (AE) have included abdominal pain, diarrhea, and asthenia. Pulmonary emboli have occurred in 6 patients (asymptomatic in 4, death in 1). Grade 3 hypertension or hand -foot syndrome occurred in <5% of patients. 12% of patients discontinued study treatment due to tel related AEs.

Conclusion: Tel-XP resulted in rapid disease control within 2 cycles, with substantial antitumor responses that appear durable. The combination was well tolerated, and does not appear to increase toxicity substantially compared to the doublet chemotherapy alone. The drug profile allows continuous inhibition of angiogenesis without increase in off target toxicities.

Disclosure: All authors have declared no conflicts of interest.

724P PROGNOSTIC SIGNIFICANCE OF FREE PERITONEAL TUMOR CELLS (FPTCS) IN THE PERITONEAL CAVITY BEFORE AND AFTER NEOADJUVANT CHEMOTHERAPY IN PATIENTS WITH GASTRIC CARCINOMA UNDERGOING A POTENTIALLY CURATIVE RESECTION

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Background: FPTCs are an independent prognostic factor in patients undergoing curative resection for gastric carcinoma. Whether neoadjuvant chemotherapy (NAC) can eliminate FPTCs in the peritoneal lavage remains unclear. The aim of the study was to determine the effect of NAC on FPTCs.

Methods: From 1994-2000, a total of 61 patients with resectable gastric cancer were analysed. Peritoneal cytology was performed before NAC at laparoscopy and at tumor resection. A minimum of six weeks of NAC, consisting of cisplatin, folinic acid and fluorouracil was administered. FPTCs were detected immunhistochemically using Ber-EP4 antibody.

Results: No FPTCs could be detected in 42 patients (69%), compared to 19 (31%) with FPTCs before NAC. During chemotherapy 10/42 patients (24%) developed FPTCs and 7/19 patients (37%) reverted from positive to negative. Patients who became FPTC negative (n=7) showed an improved median survival (36.1months) and a longer 2-year survival (71.4%) compared to FPTC positive patients before and after NAC (n=12), with a median survival of 9.2months and a 2-year survival rate of 25%. In contrast, patients who reverted from FPTC negative to positive during NAC (n=10) had a median survival of 18.5 months and a 2-year survival of only 20%. Multivariate analysis identified ypN category and FPTC change as independent prognostic factors.

Conclusions: NAC for patients with positive cytology could lead into FPTC negativity in a subset of patients and to improve their prognosis. However, NAC might be a risky strategy for almost one-quarter of patients who develop positive cytology.

Disclosure: All authors have declared no conflicts of interest.

725P PHASE II STUDY OF EVEROLIMUS IN PATIENTS WITH ADVANCED GASTRIC CANCER REFRACTORY TO CHEMOTHERAPY INCLUDING FLUOROPYRIMIDINE AND PLATINUM

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Background: To evaluate feasibility with activity and toxicities of everolimus, a novel inhibitor of mammalian target of rapamycin (mTOR), in patients with advanced gastric cancer (AGC) who failed chemotherapy including both fluoropyrimidine and platinum (FP) agents.

Methods: Fifty-four patients were enrolled between July 2008 and February 2010. 10mg daily, was given until disease progression or unacceptable toxicity. Primary end point was to determine 4-month progression-free survival (PFS) and secondary end points were to investigate response rate, toxicity and overall survival (OS) rate.

Results: In addition to FP, 19 patients were refractory to docetaxel and two failed irinotecan, respectively. A total of 180 cycles of everolimus were administered with a median of 2 (range, 1-20) cycles in each patient. Two patients (3.7%) achieved confirmed partial response and 19 patients (35.2%) showed stable disease, resulting in a disease control rate of 38.9%. At a median follow-up duration of 8.7 months in surviving patients (range, 3.0 – 19.4 months), a 4-month PFS rate was 18.4% with a median PFS of 1.7 months (95% confidence interval [CI], 1.5-2.2 months) and a median OS time was 8.3 months (95% CI, 4.5-12.1 months). Peritoneal metastasis was significantly associated with shorter PFS time (Hazard ratio, 3.97; 95% CI, 1.54-10.23; p=0.010). Treatment was in general well tolerated. Grade 3/4 anemia and thrombocytopenia occurred in 9.4% of patients, respectively but no grade 3/4 neutropenia was observed. Non-hematologic toxicities of grade 3 or higher included hepatic dysfunction (11.3%) and pulmonary toxicities (one interstitial pneumonitis and a diffuse alveolar hemorrhage [DAH] case). The DAH and cardiopulmonary dysfunction in another case resulted in treatment-related mortalities. Dose reduction was required in five patients and seven discontinued treatment due to adverse events or intolerance to everolimus.

Conclusions: Everolimus monotherapy showed modest activity against heavily pretreated AGC. The toxicity profile was generally mild. However, careful monitoring for treatment-related pulmonary complication seems to be required.

Disclosure: Y. Kang: honorarium and consultant for Novartis. All other authors have declared no conflicts of interest.

726P HELICOBACTER PYLORI INFECTION AS AN INDEPENDENT PROGNOSTIC FACTOR FOR LOCALLY ADVANCED GASTRIC CANCER PATIENTS TREATED WITH ADJUVANT CHEMOTHERAPY AFTER CURATIVE RESECTION

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Purpose: A few studies reported the association between negative helicobacter pylori (H. pylori) infection and poor clinical outcome in resected gastric cancer patients.

Patients and methods: We investigated the H. pylori infection status and its association with the clinical outcome in 274 locally advanced gastric cancer patients (stage IB: 25, II: 82, IIIA: 80, IIIB: 39, IV: 48) who underwent adjuvant chemotherapy after curative resection (>=D2 dissection). H. pylori infection status in hematoxylin and eosin stained corporal and antral mucosa of non-tumor tissue was graded

according to the updated Sydney System and categorized as H. pylori negative (normal or mild infection) and H. pylori positive (moderate or marked infection). Eighty-one patients received 5-FU and doxorubicin-based chemotherapy, while 193 patients underwent 5-FU, mitomycin-C, and polysaccharide-K chemotherapy.

Results: The median follow-up duration of survivors was 144 (120-184) months. In univariate analysis, patients with H. pylori negative (108 pts) demonstrated significantly poor 10-year overall survival compared with those with H.pylori positive (166 pts) (21.3% vs. 71.1%, p<0.0001). H. pylori negative status was associated with poor outcome in all stages except stage IIIB. In multivariate analysis, H. pylori negative status was the most significant independent prognostic factor of poor overall survival (hazard ratio: 3.45, 95% CI: 2.43-4.89, p<0.0001) followed by old age (p<0.0001), advanced stage (p=0.001), and Bormann type IV (p=0.027).

Conclusion: H. pylori infection status seems to have strong prognostic significance in locally advanced gastric cancer. H. pylori negative patients may need intensified adjuvant treatment and careful follow-up after curative resection.

Disclosure: All authors have declared no conflicts of interest.

727P EXPRESSION OF BAX PREDICTS OUTCOME IN ADVANCED GASTRIC CANCER PATIENTS TREATED WITH 5-FLUOROURACIL AND PLATINUM PALLIATIVE CHEMOTHERAPY

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Purpose: The present study evaluated the predictive role of Bax, excision repair cross-complementation group 1 (ERCC1), and thymidylate synthase (TS) on clinical outcomes in patients with advanced gastric cancer treated with 5-fluorouracil (5-FU) and platinum palliative chemotherapy.

Materials and methods: One hundred and twenty-eight patients with metastatic or recurrent gastric cancer were treated with a chemotherapy regimen of either 5-FU and heptaplatin (FH) (56 patients) or 5-FU, leucovorin, and oxaliplatin (FOLFOX) (72 patients). Pretreatment tumor biopsy specimens were analyzed for Bax, ERCC1, and TS expression by immunohistochemistry.

Results: High expression of Bax, ERCC1 and TS was observed in 49 (38%), 60 (47%), and 48 (38%) patients, respectively. The median overall survival (OS) of patients in total was 10 months. Low expression of Bax was associated with poor OS (median, 9 months vs. 12 months; 2-year, 7% vs. 32%; p=0.0005) in univariate analysis, while expression of ERCC1 and TS was not correlated with patient outcome. The outcome of patients with low expression of Bax was significantly worse in the FOLFOX group (median OS, 9 months vs. 18 months; p=0.0008), without significant difference in the FH group. In multivariate analysis, low expression of Bax was a significant independent predictor of poor OS (p=0.014).

Conclusions: Low expression of Bax was significantly associated with the poor survival of patients with metastatic or recurrent gastric cancer treated with 5-FU and platinum chemotherapy. Immunohistochemical staining for Bax with pretreatment biopsy specimen may be useful in selecting FOLFOX regimen as a treatment option for these patients.

Disclosure: All authors have declared no conflicts of interest.

728P MICRORNA-196B AND MICRORNA-363 WERE IDENTIFIED AS GASTRIC CANCER SPECIFIC MICRORNAS IN HUMAN GASTRIC CANCER TISSUE USING MICROARRAY EXPERIMENT

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Background: MicroRNAs regulate gene expression post-transcriptionally by degradation or inhibition of translation of target mRNA through which regulate cell proliferation and apoptosis, and play a role in the pathogenesis of various human cancers. Here we investigated gastric cancer specific microRNAs in human gastric cancer samples.

Method: We performed microRNA microarray experiments in 60 fresh frozen gastric cancer samples and 8 normal surrounding tissues. Total RNA was extracted and microarray experiments were performed according to the manufacturer's protocols. The microarray data were normalized. Gastric cancer specific miRNAs were extracted through two tailed t-test (p<0.01). The obtained results were validated with quantitative reverse transcription-PCR in another paired 12 patients samples. MiRecords (http://mirecords.umn.edu/miRecords) was used as bioinformatics tools for screening predicted miRNA target genes. The results were combined with gene expression microarray data which came from same patient samples.

Results: 19 microRNAs were highly expressed (>2-fold change) in gastric cancer tissue and 18 were down regulated (< 0.5 fold change) compared to non-tumor tissue. Out of 37 gastric cancer specific microRNAs, four microRNAs including miR-135b, miR-196b, miR-363, and miR-193a-3p were validated by quantitative reverse transcription-PCR. miR-196b and miR-363 showed statistically significant results (p = 0.007 and 0.0001, respectively) in two sample paired t-test. Common genes which expression were negatively correlated with microRNA expression (Pearson correlation, p<0.005) and also identified as predicted targets using microRNA target searching programs were regarded as target gene candidates in specifically gastric cancer. Using this method, we could indentify 260 and 74 target genes of miR-196b and miR-363, respectively

Conclusions: MiR-196b and miR-363 were revealed as gastric cancer specific microRNAs using microarray experiment. Among target candidate genes of theses microRNAs, ADAM15 was most reliable target gene of miR-363. It is worthy to validate the relation of ADAM15 and miR-363 or gastric cancer.

Disclosure: All authors have declared no conflicts of interest.

729P MRNA EXPRESSION OF BRCA1, RAP80 AND SUMO LIGASES (PIAS1 AND PIAS4) AND SURVIVAL IN GASTRIC CANCER PATIENTS (P) RECEIVING SECOND-LINE DOCETAXEL (DOC)

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Background: BRCA1 and RAP80 are implicated in response to chemotherapy, and SUMO pathway components (PIAS1, PIAS4) are required in DNA damage repair. PIAS1 influences BRCA1 and RAP80 accumulation, and PIAS4 is involved earlier in DNA damage response. The involvement of the SUMO pathway in DNA damage response could mean that alterations of SUMOylated proteins could have a dramatic response on chemotherapy response.

Methods: We have examined the expression of BRCA1, RAP80, PIAS1 and PIAS4 by RT-QPCR in 133 advanced gastric cancer p treated with FOLFOX, 59 of whom received second-line doc.

Results: Median age: 74 p not receiving doc, 64 years; 59 receiving doc, 58 years (P=0.05). No other differences in baseline characteristics were observed. 102 males; 41 stage IIIA, 41 stage IIIB, 51 stage IV. A good correlation between the expression of the four genes was observed (P<0.001). Median survival (MS) was 12.5 months (m) overall. For the 59 p receiving doc, MS was 24.9 m for p with high BRCA1 levels and 9.5 for p with low BRCA1 levels (P=0.002), 19.1 m for p with high PIAS1 and 9.5 for p with low PIAS1 (P=0.03). In the multivariate analysis, shorter MS was seen in p not receiving second-line doc (HR, 1.82; P=0.01) and in stage IV p (HR, 2.63; P=0.002), and longer MS was seen in p with high PIAS1 levels (HR, 0.45; P=0.004).

Conclusions: Alterations in BRCA1 SUMOylation could predict outcome to chemotherapy. Trials of customized chemotherapy based on the levels of BRCA1 and PIAS1 could help to optimize treatment in gastric cancer p.

Disclosure: All authors have declared no conflicts of interest.

730P SUVMAX OF F-18 FDG-PET/CT IN ADVANCED GASTRIC CANCER WITH TUBULAR ADENOCARCINOMA: CORRELATION WITH PATHOLOGIC FINDINGS INCLUDING IMMUNOHISTOCHEMICAL STAINING

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Background: The role of F-18 FDG-PET/CT in gastric cancer is limited because of its low sensitivity, which ranges from 78% to 93% in advanced gastric cancer (AGC). This retrospective study was designed to assess the accuracy of F-18 FDG-PET/CT in AGC with tubular adenocarcinoma and its correlation with other pathologic findings including immunohistochemical staining.

Methods: One hundred and fifty two patients with AGC (age=63.0±10.4 years, M:F=106:46) who underwent F-18 FDG-PET/CT 1 month before operation were included for this study. They were divided into 3 groups according to the SUVmax of the tumor. All patients were reviewed medical records including immunohistochemical staining results. All parameters were compared among 3 groups by one-way ANOVA and χ^2-test.

Results: The mean SUVmax was 8.19 in AGC with tubular adenocarcinoma. Group 1 was 62 patients with tumor SUVmax lower than 5, group 2, 53 patients with SUVmax 5.0–9.9 and group 3, 37 patients with SUVmax ≥10. The intensity of FDG uptake was correlated with tumor size (r^2=0.352, p<0.001) and GLUT-1 expression (r^2=0.225, p<0.006). The intensity of FDG uptake showed significant difference with T stage, N stage, GLUT-1 expression, and Ming and Lauren classification. SUVmax was higher in expanding type of Ming and intestinal type of Lauren. And all of the immunohistochemical parameters including p53, Ki-67, C-erbB-2, Rb, EGFR and tumor differentiation were not related to the degree of SUVmax.

Conclusions: Preoperative tumor SUVmax of F-18 FDG-PET/CT in AGC with tubular adenocarcinoma was correlated with tumor size, T and N stage, GLUT-1 expression and Ming and Lauren classification.

Disclosure: All authors have declared no conflicts of interest.

731P PREDICTIVE FACTORS FOR ADJUVANT THERAPY IN PATIENTS WITH LOCALIZED GASTRIC and GASTRO-ESOPHAGEAL JUNCTION (G/GEJ) CANCER: A POPULATION BASED STUDY

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Background: Adjuvant chemo-radiation therapy (CRT) results in significant improvement in survival of patients with high risk gastric and gastro-esophageal junction (G/GEJ) cancer. Little is known about the predictive factors of adjuvant CRT in such patients. Our study aims to determine predictive markers for adjuvant CRT in patients with localized G/GEJ cancer and to identify factors that correlate with survival.

Methods: Medical records of patients with localized G/GEJ cancer diagnosed between 2002 and 2007 in the province of Saskatchewan were reviewed. Logistic regression analysis was done and various clinico-pathological factors were examined to identify predictive markers for adjuvant CRT. A Cox proportional hazards models was done to determine prognostic markers with respect to survival.

Results: 162 eligible patients with median age of 70 yrs and M:F of 65:35 were identified. 51% patients had ECOG PS of 0. 66% patients had gastric cancer, 54% had stage IB and II disease and 37% had node negative disease. Of 162 patients 34% received adjuvant CRT. Of 102 patients who did not receive adjuvant CRT, 32% patients were not referred for CRT, 44% patients were not found to be optimal candidate, and 24% declined adjuvant CRT. On multivariate analysis positive resection margin (HR 2.9; 95% CI: 1.0-8.4), stage 3 and 4 disease (HR 2.4; 95% CI: 1.1-5.2), and high grade tumor (HR 2.3; 95% CI: 1.0-5.0) were correlated with adjuvant CRT. Median survival of patients who received adjuvant CRT was 32 months compared with 22 months of patients who did not received CRT (p=0.09). On multivariate analysis node negative disease (HR 0.35; 95%CI: 0.17-0.72), adjuvant CRT (HR 0.38; 95%CI: 0.22-0.66), R0 resection (HR 0.51; 95%CI: 0.28-0.92), and ECOG PS 0 (HR 0.52; 95%CI: 0.32-0.84) correlated with a superior survival.

Conclusions: Nearly two third patients did not receive adjuvant therapy. Half of the patients were not referred or declined adjuvant therapy. Positive resection margin, stage 3 and 4 disease, and high grade tumor were identified as predictive markers for adjuvant therapy. ECOG PS, adjuvant therapy, resection margin and lymph node status correlated with progosis in such patients.

Disclosure: All authors have declared no conflicts of interest.

732P PROGNOSTIC IMPACT OF IMMUNOHISTOCHEMICAL EXPRESSION OF KI-67 IN PATIENT WITH ADVANCED GASTRIC CANCER WHO UNDERWENT CURATIVE RESECTION

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Background: Ki-67, tumor proliferation marker, in an important prognostic factor in a variety of cancers. In the present study, we investigated the prognostic value of immunoexpression of Ki-67 in patient with gastric cancer who underwent curative resection.

Material and methods: We retrospectively analyzed 241 patients who had undergone curative gastrectomy at Gachon University Gil Hospital between January 2008 and July 2009. Ki-67 proliferation index (PI) by immunohistochemistry on formalin-fixed, paraffin-embedded material and the other clinicopathologic variables were evaluated by univariate and mulvariate analysis.

Results: The median follow-up from surgery was 12 months (range, 0.5-26.7 months) and mean recurrence-free survival was 23 months (95% confidence interval, 21.8-24.1 months). The mean Ki-67 PI was 40% (range, 5-90%). No significant correlation was found between Ki-67 PI and other clinicopathologic variables including histologic grade and pathologic TNM (pTNM) stage. Univariate analysis revealed that significant prognostic factors of recurrence-free survival included age, pre-operative serum albumin, pre-operative hemoglobin, surgery type, pTNM, histologic grade, lymphatic vessel invasion, peri-neural invasion, and Ki-67 PI. In the multivariate analysis besides pTNM (p=0.046), lymphatic vessel invasion (p=0.024), and surgery type (p=0.047), Ki-67 PI (p=0.005) also remained as an independent prognostic factor of recurrence, whereas the other factors lost its prognostic value.

Conclusions: Our results suggested that high Ki-67 PI was independent, poor prognostic factor of recurrence in patient with gastric cancer who underwent curative resection.

Disclosure: All authors have declared no conflicts of interest.

733P PREDICTIVE SIGNIFICANCE OF PREOPERATIVE PERIPHERAL BLOOD VALUES FOR STAGE T4 GASTRIC CANCER

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Background: The preoperative diagnostic accuracy of gastric cancer staging is remained to be established. We explored the predictive significance of peripheral blood values in patients with surgical intervention.

Method: 304 patients with advanced gastric cancer undergoing surgery from 2002 to 2005 were indentified retrospectively from database. The classification was based on the international Union Against Cancer (seventh edition). Advanced gastric cancer was defined deeper wall invasion than muscularis propria (≥T2). Patients receiving neoadjvant chemotherapy were excluded. T stage and nodal status were compared to preoperative hematological and biochemical parameters. Subsequently the predictive value for stage T4 was evaluated by multiple logistic regression analysis.

Result: In total of 304 cases, the median age was 64 years old, 209 (68.8%) were male and 95 (31.2%) were female. All was estimated indication to curative resection before surgery. The curative resection was accomplished in 264 (86.8%) whereas the distant metastasis was diagnosed on laparotomy in 40 (13.2%). Depth of primary lesion was assessed as stage T2 in 78 (25.7%), stage T3 in 127 (41.8%) and stage T4 in 99 (32.6%). Elevated neutrophil/lymphocyte (N/L) ratio, platelet/lymphocyte (P/L) ratio and serum CRP and decreased lymphocyte count, hemoglobin, serum total protein and serum albumin were significantly correlated with stage T4 respectively. Odds ratio for N/L (OR=1.892 95%CI, 1.034-3.463, p=0.039) and serum CA19-9 (OR=2.927 95%CI, 1.429-5.997, p=0.003) were suggested significant predictive values for stage T4.

Conclusion: Preoperative values of N/L and serum CA19-9 may be reliable factors to assess preoperative staging in advanced gastric cancer.

Disclosure: All authors have declared no conflicts of interest.

734P SURVIVAL BENEFIT OF GASTRECTOMY ± METASTASECTOMY IN METASTATIC GASTRIC CANCER PATIENTS RECEIVING CHEMOTHERAPY

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Background and Objectives: To investigate the role of surgery in gastric cancer (GC) with distant metastasis.

Methods: Newly diagnosed 274 GC patients with synchronous metastases who had received chemotherapy were categorized into 3 groups according to applied surgical treatment: complete gross resection of both primary and metastatic sites (group A; n = 42), debulking gastrectomy (group B; n = 47) and chemotherapy without debulking (group C; n = 185).

Results: Median overall survival (OS) of all patients was 11.8 months. Median OS and 3-year survival rate were 28.0, 15.5 and 9.0 months and 42.8%, 8.1% and 3.5% in groups A, B and C, respectively. In group A, patients with peritoneal seeding, intra-abdominal distant lymph nodes, ovarian or hepatic metastases underwent complete gross resection and 12 (29%) had no evidence of recurrence at the time of last analysis (median follow-up duration, 29.1 months). In multivariate analysis, the adjusted hazard ratios for death

Conclusions: Our study suggests survival benefits of debulking gastrectomy or gastrectomy plus metastasectomy in GC patients with distant metastasis.

Disclosure: All authors have declared no conflicts of interest.

735P 10-YEAR FOLLOW-UP OF GASTRIC SUBMUCOSAL TUMORS

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Background: Gastric Submucosal tumors (SMTs) were incidentally discovered endoscopical or radiological examination. However, they have not been studied in detail of epidemiology or treatment strategy for SMTs. The aim of this study is to clarify the clinical features and long-term outcomes of gastric SMTs.

Methods: A data base was established by endoscopic medical records from January to December 1998 in Aichi Cancer Centre. All clinical data of gastric SMTs were collected:

size, location, and clinical courses. This retrospective review was conducted for 10-year period in every SMT.

Results: We performed 5307 EGDs and detected 188 gastric SMTs (3.5%; 81 males, 107 females) during one year. Majority of SMTs was less than 1cm (64%) and SMTs<2cm were 91%. 56% of SMTs located middle one third of stomach, and the remaining SMTs were equally detected at upper (22%) and lower (22%), respectively. Sixteen SMTs were ≥2cm and fifteen were monitored for 10 years. 4 cases underwent surgery because two (leiomyosarcoma) was ≥5cm, one (GIST) enlargement and one (GIST) simultaneously resected with gastrectomy for gastric cancer. One leiomyosarcoma appeared liver metastases. 172 SMTs were <2cm and 156 followed for ten years. Three SMTs were enlarged: two underwent surgery and one followed because enlarged size was <1cm. Two resected SMTs were GIST and one of them was recurred. Observed pts <2cm were detected no SMT related death.

Conclusions: The incidence of SMTs is 3.5%, majority (91%) is small (<2cm), and frequent location is middle one third of stomach. Large size (≥5cm) and enlargement might be malignant features of SMTs.

Disclosure: All authors have declared no conflicts of interest.

736P DEVELOPMENT OF A COMPREHENSIVE REGISTRY OF GASTROINTESTINAL STROMAL TUMOR (GIST) PATIENTS (PTS) IN EASTERN ONTARIO

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Background: Targeted therapy of GISTs with Imatinib mesylate (IM) has revolutionized therapy of recurrent and metastatic tumors. In addition there is an emerging role for IM as adjuvant therapy. Subclassification of GISTs according to kinase mutations status has both biological and clinical implications, since it predicts response to Imatinib and prognosis following resection.

Methods: We have undertaken a study of all patients diagnosed with GISTs at The Ottawa Hospital between 2004-2009. Data included pt demographics, clinical characteristics, treatment and clinical outcomes. Pathologic assessment included tumor size and location, number of mitoses/50HPF, and exhaustive immunohistochemistry stains including CD117, DOG1, CD34, vimentin, S100, desmin, SMA and caldesmon. Risk stratification was performed using Miettinen criteria. Molecular classification was performed in all cases at a central laboratory. DNA was obtained from formalin fixed paraffin-embedded archived material. PCR amplification and sequencing was done for exons 9, 11, 13, 17 of KIT and exons 12 and 18 of PDGFRA genes.

Results: A total of 52 cases have been identified. 31 (60%) involved stomach, 15 (30%) small bowel, 3 (5%) rectum, 2 (4%) esophagus, and 1 (2%) colon. Using Miettinen criteria relapse risk was: very low: 2 (4%), low: 29 (56%), intermediate: 4 (8%) and high risk: 17 (32%). Overall, 32 (62%) were treated with surgery only and 20 (38%) received adjuvant IM. On average, those who received adjuvant IM were treated for 12 months. 11 (21%) developed metastases, 5 (10%) recurred locally or regionally, and 2 (4%) died of disease. Mutational analysis was performed in 45 tumors with the following results: KIT mutation frequencies: exon 11: 23 (44%), exon 9: 3 (5%), and exon 17: 1 (2%); PDGFRA mutations- exon 18: 3 (5%), exon 12: 1 (2%). Wild type: 15 (29%). Mutational analyses in 11 patients who developed metastases will be presented.

Conclusions: In rare tumors such as GISTs, with rapidly shifting treatment paradigms, comprehensive, centralized regional, collaborative databases are feasible and compulsory to assess short and long term outcomes of interventions.

Disclosure: All authors have declared no conflicts of interest.

737P COST-EFFECTIVENESS OF ADJUVANT IMATINIB IN PATIENTS WITH SURGICALLY RESECTED LOCALIZED GASTROINTESTINAL STROMAL TUMORS (GIST): CANADIAN SOCIETAL PERSPECTIVE

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Background: Treatment with adjuvant imatinib following surgical resection of localized GIST has been shown to increase recurrence-free survival (RFS) compared with surgical resection alone (SRA) in patients who are at intermediate to high risk of relapse. The objective of this study was to evaluate the cost-effectiveness of treatment with adjuvant imatinib in Canada.

Methods: A lifetime Markov model predicts patients' transitions across health states defined by initial treatment (adjuvant imatinib versus SRA). Recurrence rates are based on data from the ACOSOG Z9001 study. Two scenarios were evaluated: (1) 1-year scenario where 1-year trial results were used to calculate first year recurrence rates for imatinib and SRA. For subsequent years of the model the recurrence rate for imatinib are set equal to SRA and, (2) continuous scenario where recurrence rates for imatinib and SRA at the end of one year are continued over the lifetime. The model estimates direct and indirect costs (lost earnings due to early mortality and short-term disability), life-expectancy, quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios (ICER). Results are from the societal perspective in $2009 Canadian and discounted at 5% per annum. Deterministic and probabilistic sensitivity analyses (DSA and PSA) were performed to assess the impact of parameter uncertainty on model results.

Results: Adding imatinib was estimated to result in a gain of 0.745 and 5.180 QALYs at an additional expected per-patient lifetime cost of $26,800 and $326,000 for the 1-year and continuous treatment scenarios, respectively. Corresponding ICERs per QALY were therefore $36,000 and $63,000. In the DSA, model results were most sensitive to recurrence rates. Overall, results remained consistent in the PSA; 95% CI for ICERs were $31,600 to $39,400 for the 1-year and $60,400 to $65,000 for the continuous treatment scenario.

Conclusions: Results of this evaluation suggest that, from a Canadian health care system perspective, imatinib is cost-effective and represents good value for the money according to currently accepted standards of cost effectiveness.

Disclosure: V. Pawar, J. Rubin and D. Taylor: Paid consultant to Novartis Pharmaceuticals; K. El Ouagari and J.H. Coombs: Employee of Novartis Pharmaceuticals.

738P PATIENT PREFERENCES FOR REDUCING TOXICITIES OF TREATMENTS FOR GASTROINTESTINAL STROMAL TUMOR (GIST): A CONJOINT ANALYSIS STUDY

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Objectives: To quantify GIST patients' preferences for reducing treatment toxicities and the likely effect of toxicities on patients' stated adherence.

Methods: English-speaking members of the Life Raft Group, a GIST patient advocacy and research organization, aged 18 years and over completed a web-enabled survey that presented a series of treatment-choice questions, each including a pair of hypothetical GIST medication toxicity profiles. Each profile was defined by common or concerning toxicities verified via pre-test interviews including: severity of edema, diarrhea, nausea, fatigue, rash, hand-foot syndrome, and heart failure, or risk of serious infection. Each subject answered 13 choice questions based on predetermined experimental design with known statistical properties. Subjects were asked to rate the likelihood that they would miss or skip doses of medications with different toxicity profiles. Random-parameters logit was used to estimate a relative preference weight for each level of each toxicity. The study underwent IRB review and approval and subjects provided informed consent.

Results: 173 subjects completed the survey. Over the ranges of attribute levels included in the study, heart failure was the most important attribute and was assigned an importance weight of 10. Relative to heart failure, remaining attributes were ranked in order of importance.

§ Attribute	Importance Weight	
	Mean	95% CI
Heart failure	10.0	7.7-12.3
25% chance of serious infection	6.8	4.8-8.7
Nausea	5.8	4.4-7.3
Diarrhea	4.8	3.4-6.1
Hand-foot syndrome	4.3	3.1-5.6
Fatigue	3.4	2.3-4.5
Rash	3.3	2.1-4.4
Edema	3.1	2.0-4.2

For all attributes, reducing severity of toxicities from severe to moderate was more important to subjects than reducing severity from moderate to mild. Reducing heart failure from moderate to mild and diarrhea from severe to moderate had the largest effects on subjects' evaluation of adherence.

Conclusions: All toxicities and risks included in the study are important to patients. Treating or reducing severe toxicities is much more important to GIST patients than treating or reducing moderate toxicities. Focused reductions of certain toxicities may improve treatment adherence.

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739P RANDOMIZED CROSS-OVER AIO PHASE III TRIAL COMPARING GEMCITABINE PLUS ERLOTINIB FOLLOWED BY CAPECITABINE VS. CAPECITABINE PLUS ERLOTINIB FOLLOWED BY GEMCITABINE IN ADVANCED PANCREATIC CANCER

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Background: Gemcitabine (G), capecitabine (C) and erlotinib (E) are active drugs in advanced pancreatic cancer (APC); only a limited number of prognostic and predictive (molecular) factors has been defined in APC to date.

Methods: Within a prospective multicenter phase III trial, 281 patients (pts) with pathologically confirmed APC were randomly assigned to first-line treatment with either C (2000 mg/m^2/d, d1-14 q3w) plus E (150 mg/d) or G (1000 mg/m^2 over 30 min weekly x 7, then d1, 8, 15 q4w) plus E (150 mg/d). In case of treatment-failure (e.g. disease progression or toxicity), pts were ''crossed-over'' to second-line treatment with the comparator cytostatic drug without E. The primary study endpoint was time-to-treatment failure after second-line therapy (TTF2). Subgroup analyses on clinical (stage of disease, smoking status, skin rash, hand-foot syndrome, HFS) and molecular (KRAS mutation [n=176], EGFR intron 1 polymorphism (PM) [n=187]) parameters were performed.

Results: TTF2 was estimated with 4.4 months (mo) for CE-G and 4.2 mo for GE-C (HR 0.98, p=0.43), median OS was 6.9 mo and 6.6 mo (HR 0.96, p=0.78), respectively. Pts with locally advanced disease (n=47) showed a prolonged TTF2 (HR 0.56, p=0.00054) and OS (HR 0.56, p=0.0011) compared to pts with metastatic APC. Development of skin rash (any grade) during first-line E treatment (HR 0.54, p<0.0001) and KRAS wildtype (HR 0.62, p=0.011) were both associated with an improved OS. A shorter number of allele sum for CA repeats (< 36 vs. ≥ 36) in the intron 1 of the EGFR gene had no impact on OS. No correlation was found between KRAS status or EGFR intron 1 PM and the occurrence of skin rash. Never/former smokers were more likely to develop skin rash during E compared to current smokers (any grade: 73% vs. 54%; grade 2-4: 46% vs. 19%). Pts with treatment-associated HFS had an improved TTF2 (HR 0.61, p=0.00042) and OS (HR 0.66, p=0.0051). **Conclusion:** Wildtype KRAS status (but not EGFR intron 1 PM) was associated with an improved OS. Treatment-related side effects (skin rash, HFS) may be correlated with an improved therapeutic effect in terms of OS.

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740P 5-FLUOROURACIL/LEUCOVORIN (5FU/LV) COMBINED WITH IRINOTECAN AND OXALIPLATIN (FOLFIRINOX) AS SECOND LINE CHEMOTHERAPY IN PATIENTS WITH METASTATIC PANCREATIC ADENOCARCINOMA

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Background: To evaluate efficacy and toxicity of irinotecan and oxaliplatin plus fluorouracil and leucovorin (Folfirinox) as second line therapy in metastatic pancreatic adenocarcinoma (MPA).

Patients and methods: We analyzed retrospectively medical records of 27 patients with MPA treated by Folfirinox as second line therapy between January 2003 and November 2009 in our hospital. The recommended schedule was oxaliplatin 85 mg/m2 d1 + irinotecan 180 mg/m2 d1 + leucovorin 400 mg/m2 d1 followed by 5-fluorouracil 400 mg/m2 bolus d1 and 2400 mg/m2 46h continuous infusion biweekly.

Results: Pts characteristics: M/F=13/14; median age = 63 years [45-83]. All patients had a progressive disease after first line chemotherapy by gemcitabine. Safety: A total of 167 cycles were delivered, with a median number of 6 cycles [1-29] per patient. One toxic death occurred (sepsis). Tolerance was excellent with a good respect of the dose density (Ox: 92.8%, Ir: 89.1%, 5-FU: 96.4%). Grade (G) 3-4 neutropenia occurred in 55.6% of pts, including 1 febrile neutropenia. Other toxicities were manageable. Efficacy: 22 of 29 pts were evaluable (WHO and RECIST criterias). 5 partial responses and 12 stabilizations were observed. Median progression free survival was 5.4 months [0.7- 25.48], and median event free survival was 3 months [0.5-24.9]. Median overall survival was 8.5 months [0-26].

Conclusions: These results confirmed the good safety profile and the efficacy of Folfirinox regimen in the treatment of MPA, even as a second-line. It merits to be assessed in an ongoing phase III trial.

Disclosure: All authors have declared no conflicts of interest.

741P CONATUMUMAB (CON) OR AMG 479 OR PLACEBO (PBO) + GEMCITABINE (GEM) IN PATIENTS (PTS) WITH METASTATIC PANCREATIC CANCER (MPC): A PLACEBO-CONTROLLED, RANDOMIZED, PHASE 2 STUDY

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CON, a human death receptor 5 agonist, and AMG 479, an insulin-like growth factor receptor 1 antagonist, are investigational, fully human monoclonal antibodies. A 3-arm, placebo (pbo)-controlled, randomized phase 2 study evaluated both agents in mPC. The study (planned sample size = 120) was designed to estimate the efficacy of adding CON or AMG 479 to gem vs pbo. Eligibility included no prior therapy for mPC, PS 0-1, and no poorly controlled diabetes. Pts were randomly allocated 1:1:1 to Arm 1: CON + gem (double-blinded); Arm 2: AMG 479 + gem (open-label due to anticipated thrombocytopenia and hyperglycemia); Arm 3: pbo + gem (double-blinded). Pts

Abstract: 741P

	CON + Gem (Arm 1)	AMG 479 + Gem (Arm 2)	Pbo + Gem (Arm 3)	Arm 1 vs 3	Arm 2 vs 3
6-mo OS (95% CI)*	59% (42, 73)	57% (41, 70)	50% (33, 64)	10% (-12, 31)	6% (-16, 27)
12-mo OS (95% CI)	20% (9 34)	39% (25, 54)	23% (11, 38)	-3% (-23, 16)	15% (-5, 35)
OS events	32 (78%)	29 (69%)	34 (81%)	-	-
Median OS (95% CI), mo	7.5 (4.8, 10.0)	8.7 (5.3, 12.2)	5.9 (4.1, 9.7)	HR = 0.87 (0.53, 1.43); p = 0.59	HR = 0.67 (0.41, 1.12); p = 0.12
PFS events	38 (93%)	37 (88%)	38 (90%)	-	-
Median PFS (95% CI), mo	4.0 (3.3, 5.0)	5.1 (2.8, 5.8)	2.1 (1.9, 3.3)	HR = 0.65 (0.41, 1.05); p = 0.08	HR = 0.65 (0.41, 1.04); p = 0.07
Objective response	1/38 (3%)	4/39 (10%)	1/40 (3%)	-	-
Stable disease	22/38 (58%)	16/39 (41%)	15/40 (38%)	-	-

*Primary endpoint. Data cut off, March 2010.

received CON 10 mg/kg, AMG 479 12 mg/kg, or pbo IV days (D) 1 and 15 and gem 1000 mg/m^2 IV over 30 min D 1, 8, 15 Q 28 D. Randomization was stratified by PS (0 vs 1). CT scans were done Q 2 cycles. Primary endpoint: 6-month (mo) overall survival (OS). 125 pts (Arms 1/2/3: 41/42/42 pts) enrolled between 3/08 and 4/09; 41/40/40 received ≥1 dose of study drug. Median age, 61/66/61 years; male, 59/60/62%; PS 1, 59/55/62%; liver metastases, 66/69/79%. See table for efficacy. Percentage of pts with grade ≥3 adverse events (Arms 1/2/3) included: neutropenia 22/18/13%; thrombocytopenia 17/15/8%; abdominal pain 17/8/13; fatigue 12/13/5%; hyperglycemia 2/18/3%. In summary, CON + gem or AMG 479 + gem was well tolerated in this pt population. AMG 479 + gem vs pbo + gem trended toward improved 6-mo OS (57% vs 50%), 12-mo OS (39% vs 23%), median OS (8.7 vs 5.9 mo), and median PFS (5.1 vs 2.1 mo). CON + gem vs pbo + gem trended toward improved 6-mo OS (59% vs 50%), median OS (7.5 vs 5.9 mo), and median PFS (4.0 vs 2.1 mo) and higher rates of stable disease (58% vs 38%). These data suggest that further study of AMG 479 + gem is warranted in advanced PC. Efficacy

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742P A PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED, GROUP SEQUENTIAL TRIAL OF POLYCLONAL ANTIBODY STIMULATOR (PAS) FOR THE TREATMENT OF ADVANCED PANCREATIC CANCER

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Background: Gastrin hormone is trophic to in vitro pancreatic cancer, and antigastrin antibodies (AGAs) are antiproliferative and antimetastatic. Human pancreatic cancers overexpress gastrin genes and receptors that react to gastrin's trophic effects. Polycloncal Antibody Stimulator (PAS) elicits a specific and high-affinity AGA.

Methods: In this randomized, double-blind, placebo controlled, group sequential trial, patients received PAS vaccination or placebo intramuscularly on Weeks 0, 1, 3 and 24. Eligible patients had histologically or cytologically confirmed pancreatic adenocarcinoma (unsuitable for curative resection) with a life expectancy >2 months. The primary endpoint of the study was overall survival (OS).

Results: Adult patients with Stage II, III, or IV pancreatic carcinoma were randomized; all patients were included in the intent-to-treat (ITT) analyses of efficacy, demography and baseline characteristics: 154 patients - 79 on PAS and 75 on placebo. In the ITT population, survival was significantly longer for the PAS group than for the placebo group (median 150 days vs 84 days, respectively; p=0.016). Secondary endpoints, e.g., Quality of Life, performance status and weight, confirmed clinical benefit in PAS treated patients. In the PAS arm, 49 patients (64.5%) mounted measurable AGAs. AGA responsiveness was positively associated with survival, a covariate independent of baseline health status. Except for injection site reactions, PAS did not have an adverse effect on safety.

Conclusions: The results demonstrated that successful treatment with PAS prolongs survival and may inhibit tumor progression, as would be expected with cytostatic therapy. Further, PAS is safe and very well tolerated in the context of cancer therapies. AGA response was an independent OS prognosticator; the analysis of survival time between patients mounting measurable AGAs and those who did not using Kaplan-Meier estimates shows statistically significant results between the patient groups. PAS provides a new therapeutic option for patients with advanced pancreatic cancer who may not be suitable for or refuse cytotoxic chemotherapy.

Disclosure: J.M. Oortgiesen, L.A. Dimichele, J.R. Weidman, A. Cato and L.Y. Sutton: I have financial interest in this product. All other authors have declared no conflicts of interest.

743P RESULTS OF A PHASE 1/2 STUDY OF NAB-PACLITAXEL PLUS GEMCITABINE IN PATIENTS WITH ADVANCED PANCREATIC CANCER WITH SPARC AND CA19-9 CORRELATIVES

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Background: Pancreatic cancer cells and surrounding stroma are known to overexpress SPARC (secreted protein acid rich in cysteine), which is associated with poor clinical outcomes. In a preclinical model, nab-paclitaxel, an albumin-bound nanoparticle form of paclitaxel, together with gemcitabine (G) has been shown to deplete the tumoral stroma and achieves higher intratumor concentrations of both therapeutic agents when administered in combination vs alone. This phase 1/2 study was designed to evaluate the safety and efficacy of nab-paclitaxel + G, correlated with SPARC and serum CA19-9 levels.

Methods: nab-Paclitaxel (100-150 mg/m^2) + G (1000 mg/m^2) were given on days 1, 8, and 15 of a 28-day cycle to previously untreated patients (pts) with metastatic pancreatic adenocarcinoma. SPARC expression signature in the tumor was evaluated for 7 components microscopically to discriminate pts with low and high risk of death.

Results: Of the 67 treated pts, the most common grade 3/4 treatment-emergent adverse event (TEAE) that occurred in >20% of pts was neutropenia and fatigue. Thirty-nine (58%) pts and 17 (25%) pts had a TEAE grade 3/4 event, respectively. Grade 3 neuropathy occurred in 9 (13) pts. By RECIST criteria, of the 67 pts evaluable to date, 3 (4%) had complete response, 28 (42%) had partial response, and 12 (18%) had stable disease ≥16 weeks. The median survival was 10.3 months (all arms), with 12.2 months in the 125 mg/m^2 arm. SPARC data were available for 36 pts. Survival was collated with SPARC signature (13.6 vs 8.1 median months in the low vs high risk, P = 0.02). All evaluable pts had an >20% decrease in CA19-9 levels, which is historically associated with improved survival.

Conclusions: The combination of nab-paclitaxel + G, in particular the 125 mg/m^2 arm, was well tolerated and produced substantial efficacy in patients with pancreatic cancer. Additionally, survival was correlated with SPARC signature in these pts. Based on these results, a phase 3 clinical trial in currently enrolling patients.

Disclosure: N. Desai: I am an employee of Abraxis BioScience and hold patent for the investigational drug; J. Iglesias: I am an employee of Abraxis BioScience. All other authors have declared no conflicts of interest.

744P EFFICACY OF CONTINUOUS INFUSED 5-FLUOROURACIL, DOXORUBICIN, AND MITOMYCIN (IFAM) IN THE TREATMENT OF GEMCITABINE-PRETREATED PANCREATIC CANCER AND ANALYSIS OF PROGNOSTIC FACTORS IN SALVAGE SETTING

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Background: Gemcitabine-based chemotherapy (GBC) is a standard first-line treatment in advanced pancreatic cancer. In gemcitabine-pretreated pancreatic cancer, salvage chemotherapy has not yet been established and the prognostic factors have not been widely known. The purpose of this study was to evaluate the efficacy and safety of iFAM in gemcitabine-pretreated pancreatic cancer and to reveal the prognostic factors.

Methods: Eligibility included: 1) age 18-75, 2) histologically confirmed pancreatic cancer 3) relapse within 6 months after adjuvant GBC or previously treated with palliative GBC, 4) ECOG PS 0-2, 5) adequate organ function. iFAM consisted of 5-FU 800 mg/m2 over 10 hour on days 1-5, doxorubicin 30 mg/m2 on day 1 and mitomycin-C 8 mg/m2 on day 1, every 4 weeks.

Results: Between Feb 2003 and Aug 2009, 60 patients (pts) were enrolled. The median age was 57.4 yrs (range: 35.4–74.1 yrs), and there were 43 men (71.7%). 40 pts (66.7%) had ECOG PS 0-1 and 20 pts (33.3%) had PS 2. The median follow-up duration was 5.2 months (range: 0.6-61.5). Median cycles of iFAM were 2 (range: 1-10). The relative dose intensity of each drug was 87.6% in 5-FU, 87.7% in doxorubicin and 87.7% in mitomycin-C. Best responses to iFAM were PR in 6 (10.0%) pts and SD in 8 (13.3%), that is response rate was 10.0% (95% CI: 2.4–17.6) and disease control rate was 23.3% (95% CI: 12.6–34.0). The median TTP and OS were 2.4 (95% CI: 2.0–2.8) months and 5.9 (95%

CI: 4.2–7.6) months, respectively. Grade 3/4 hematologic toxicities were neutropenia (3.3%) and thrombocytopenia (3.3%). Frequent non-hematological toxicities were alopecia (41.7%), stomatitis (21.6%), vomiting (11.6%) and diarrhea (11.6%), which was predominantly Gr 1/2. ECOG PS (0-1 vs 2) was significant prognostic factor for both TTP (p<0.001) and OS (p=0.029). Elevated CA 19-9 at the time of initiation of iFAM (p=0.037) and poor response to GBC (p=0.022) were poor prognostic factors for OS.

Conclusions: iFAM is an effective and safe treatment option in gemcitabine-pretreated pancreatic cancer. PS, CA19-9 and the response to previous GBC are significant prognostic factors in this salvage setting.

Disclosure: All authors have declared no conflicts of interest.

745P GEMCITABINE (G) FIXED RATE DOSE INFUSION (FDR) PLUS ERLOTINIB (E) IN PATIENTS WITH ADVANCED PANCREATIC CANCER (APC)

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Background: G (30-minute infusion) plus E improves survival in patients with APC compared with G alone. In a recent phase III trial, G-FDR showed a trend to better OS compared with standard G (6.2 vs 4.9 months, HR 0.83, p=0.04), although the study was underpowered to detect great difference in OS. In based of our previous experience with G-FDR, we decided to evaluate the combination of G-FDR plus E, after E approval for APC.

Patients and methods: Patients with previously untreated pathologically confirmed APC, locally advanced (LAPC) or metastatic (MPC), and ECOG PS 0-2 were included. G 1500 mg/m^2 was given by 150-min infusion (10 mg/m^2/min) on days 1, 8 and 15 every 28 days combined with E 100 mg/day orally. Treatment modifications for G-FDR were planned according with previously Tempero's phase II trial, and as described in prescribing information for E.

Results: 62 pts were included (36M/26F), with a median age of 63 y-o (range 37-78). ECOG PS 0/1/2: 19/40/3. LAPC/MPC: 16/46. All except one had measurable disease. ORR was 13% (8 PR), 95% CI: 4.7-21.3, and there were 34 (55%) SD. Mean relative dose intensity for G was 0.76 and 0.90 for E. Main hematologic toxicities 3/4 per pt: anaemia 12/0, thrombocytopenia 7/4, neutropenia 18/7. Acneiform rash 1/2/3 occurred in 16/16/3 pts. Other relevant adverse events were (grade 2/3/4): diarrhoea 18/3/0, mucositis 5/1/0, infection 9/8/1, thrombosis 1/4/1 and vomiting 6/4/0. There were 3 treatment-related deaths (septic shock, cholangitis and bilateral pulmonary embolism). Ten pts (all LAPC) received RT after ≤6 cycles, all with concomitant Capecitabine 825 mg/m^2 bid. In 4 pts salvage surgery were performed: 2 R0, 1 R1 and 1 R2. Median PFS was 4.9 months (95% CI: 3-6.7), 7.9 m for LAPC and 2.5 m for MPC (p=0.004). Median OS was 10 months (95% CI: 7.1-12.9), 17.5 m for LAPC and 7 m for MPC (p = 0.019). OS was significantly shorter in males (p=0.01) and in pts taking major opioids (p=0.027). There was a trend to better OS in pts who developed skin rash grade ≥2 (p=0.078).

Conclusions: In this non comparative study, G-FDR plus E is a feasible regimen in APC with an acceptable toxicity and notable activity. G-FDR seems to increase haematological toxicity compared with standard infusion.

Disclosure: All authors have declared no conflicts of interest.

746P A PROGNOSTIC MODEL TO IDENTIFY PATIENTS WITH ADVANCED PANCREAS ADENOCARCINOMA WHO COULD BENEFIT FROM SECOND LINE CHEMOTHERAPY

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Background: The role of salvage chemotherapy after first line therapy in advanced pancreatic cancer has not yet been established. We intended to identify prognostic factors for long-term survival of advanced pancreatic adenocarcinoma patients with second-line chemotherapy and to devise a prognostic model on clinical parameters.

Patients and methods: We analyzed 90 patients who had received second line chemotherapy after the failure of first line therapy in recurrent or metastatic pancreatic adenocarcinoma between August 2003 and December 2008.

Results: The median age at the time of second line chemotherapy was 61.9 years (range, 39.8-74.9), and the median ECOG performance status was 1 (0-2). Median progression free survival (PFS) and overall survival (OS) for second line chemotherapy were 2.1 and 4.5 months, respectively, with an overall response rate of 10%. In multivariate analysis, ECOG PS of 2 or more, non-responder for first line chemotherapy and albumin level of <3.5mg/dl were independent prognostic factors for decreased OS for all 90 patients. OS was estimated based on the number of adverse prognostic factors: zero or one (good prognostic group), two (intermediate group), or three (poor prognostic group). The median OSs for good (n=50), intermediate (n=24), and poor (n=16) were 5.5, 3.3, and 2.1 months, respectively (P<0.001).

Conclusion: Our result suggests that second line chemotherapy may be beneficial for overall survival in patients with ECOG PS 0-1, albumin level ≥3.5mg/dl and good response for first line chemotherapy.

Disclosure: All authors have declared no conflicts of interest.

747P EVALUATION OF PROGRESSION-FREE SURVIVAL (PFS) BY BLINDED INDEPENDENT CENTRAL REVIEW (BICR) IN PATIENTS (PTS) WITH PROGRESSIVE, WELL-DIFFERENTIATED PANCREATIC NEUROENDOCRINE TUMOURS (NET) TREATED WITH SUNITINIB (SU) OR PLACEBO

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Background: SU is an oral, multitargeted receptor tyrosine kinase inhibitor with antiangiogenic activity. In a phase III, double-blind, placebo-controlled, randomised trial in pts with advanced, well-differentiated progressive pancreatic NET, SU 37.5 mg/day continuous daily dosing resulted in clinically significant improvement in investigator-assessed PFS when compared with placebo (median, 11.4 months vs 5.5 months, respectively; hazard ratio [HR] 0.418; 95% CI: 0.263, 0.662; P=0.0001). We report here BICR results from this study.

Methods: Baseline and on-study scans and radiology data were evaluated independently according to a two-reader, two-time point lock, followed by a sequential lock read, batch mode paradigm, by independent, third party radiologists. Reading radiologists were blinded to investigator assessments and AEs; discrepancies were adjudicated by a similarly blinded and independent third radiologist.

Results: Overall, 171 pts were randomized to treatment (SU, n=86, placebo, n=85). An analysis was conducted on the first 84 pts (49% of the pt population) for whom MRI/CT scans were available (41 SU and 43 placebo). This subset of 84 pts was representative of the intent-to-treat (ITT) population with respect to demographics, baseline disease characteristics, prior treatment, on-study adverse events, and investigator-assessed PFS. PFS was the primary endpoint in this study. Treatment effect based on investigator assessment of tumour response (median PFS: SU 19.8 months vs placebo 5.8 months; HR 0.449, 95% CI: 0.218, 0.924, P=0.0249) was similar to that based on BICR (median PFS: SU 20.6 months vs placebo 6.2 months; HR 0.289, 95% CI: 0.117, 0.716, P=0.0042). BICR of this large subset of pts confirms the investigator-assessed PFS results and argues against the presence of any bias favouring SU based upon recognition of adverse events in the SU arm.

Conclusions: This independent central review of CT scans supports the clinical PFS benefit of SU in pts with pancreatic NET. BICR on the remaining pts is ongoing.

Disclosure: E. van Cutsem: Compensated consultancy for Pfizer Inc and research funding from Pfizer Inc.; S. Patyna: Employee of Pfizer Inc. with stock options; D. Klademenos: Contracted employee of Pfizer Inc.; D. Lu: Employee of Pfizer Inc. with stock options; R. Chao: Employee of Pfizer Inc. with stock options; E. Raymond: Compensated consultancy role for Pfizer Inc. All other authors have declared no conflicts of interest.

748P THERAPEUTIC SYNERGISM OF LAPATINIB AND NVP-AEW541 AGAINST HUMAN PANCREATIC TUMOUR CELLS

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Pancreatic cancer is a particularly challenging malignancy given its usually advanced stage at diagnosis and its rather limited response to treatments. Although gemcitabine is the backbone of routine therapy in advanced disease, novel drugs are urgently needed for improving the treatment of this cancer. Overexpression and activation of tyrosine kinase receptors are common features in pancreatic cancer. The aim of this study has been to evaluate if combined inhibition of EGFR, Her-2 and IGF-IR may overcome the resistances observed in monotherapy strategies. Moreover, molecular changes involved in all treatments have been also analyzed. Several human pancreatic cancer cell lines (NP9, NP18, NP29, and CP15) with variable levels of EGFR, Her-2 and IGF-IR were treated with different concentrations of the dual inhibitor of EGFR/Her2, lapatinib, and/or the IGF-IR inhibitor NVP-AEW541 and cell viabilities were determined by MTT assay. Treatments with lapatinib in combination with NVP-AEW541 resulted in dramatic increases of growth inhibition in all the cell lines tested. The potent synergy is evidenced by the coefficients of drug interaction (CDI), which ranged between 0.01 and 0.55. Flow cytometry analysis demonstrated that the combination enhanced cell cycle

arrest at G1 and apoptotic cell death. The analysis by Western Blot of proteins involved in ErbB and IGF-IR signalling pathways demonstrate that, although each drug was able to reduce slightly the phosphorylation of Akt, Erk and IRS-1, only the combined treatment caused a marked reduction of the activated status of all three effectors. In conclusion, the combined inhibition of ErB and IGF-IR may solve the resistance due to the bidirectional transactivation of these receptors, representing a very a promising therapy against an important percentage of human pancreatic tumors.

Disclosure: All authors have declared no conflicts of interest.

749P POTENTIATION OF GEMCITABINE EFFECTS WITH A CETUXIMAB AND TRASTUZUMAB COMBINATION IN A NOVEL HUMAN PANCREATIC ORTHOTOPIC MODEL

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Introduction: Treatment of pancreatic cancer remains challenging and mostly palliative. Gemcitabine and erlotinib has shown modest benefit compared with gemcitabine alone. The efficacy of anti-EGFR therapies has been probably hampered by the absence of biomarker selected strategies. Activation of compensatory pathways, such as Her-2 or IGF-IR signaling, should be considered.

Methods: From eleven tumorgrafts only one shows moderate to high levels of both EGFR and Her-2 and very low IGF-1R activity. The other models harbor null or very low EGFR and HER-2 levels (n=4) or were positive for EGFR or Her-2 but also for IGFR activity (n=6). Pancreatic tumors obtained at the time of surgery were implanted intrapancreatically in nude mice and expanded to develop cohorts of tumor bearing mice suitable for drug evaluation. Five groups of 8 mice each were treated for 7 weeks with vehicle, gemcitabine or gemcitabine combined with cetuximab, trastuzumab or both antibodies. To determine treatment effects, tumor size measurement, antibody array analysis, CD31 staining and TUNEL labeling were performed.

Results: Combination of cetuximab and trastuzumab with gemcitabine potentiated tumor growth inhibition ($p<0.05$, triple treatment vs double treatments). In comparison to double treatments, this triple combination led to a 2.1-fold increase of cell death; the vascularization of the tumors determined by CD31 staining exhibited a 2.3-fold reduction. Moreover, significant decreases in the phosphorylation levels of EGFR, Her2 and several proteins implicated in angiogenesis, such as VEGFR2, VEGFR3 and PDGFRβ, were detected. Cell migration was also affected as shown by reduced levels of activation of Src, Fyn, Fak or Paxillin.

Conclusions: Gemcitabine combined with cetuximab and trastuzumab is a promising strategy in pancreatic tumors with activated EGFR and Her-2 but without activation of IGF-1R pathway.

Disclosure: All authors have declared no conflicts of interest.

750P EFFICACY AND SAFETY OF SORAFENIB (SOR) IN PATIENTS (PTS) WITH ADVANCED HEPATOCELLULAR CARCINOMA (HCC): SUBGROUP ANALYSES OF THE SHARP AND ASIA-PACIFIC (AP) TRIALS BY BASELINE (BL) TRANSAMINASE (ALT/AST)/ALPHA-FETOPROTEIN (AFP) AND BILIRUBIN (BIL) LEVELS

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Introduction: We examined the effect of Sor on hepatic function as indicated by Bil levels, and performed subset analyses of the SHARP and AP trials according to BL levels of ALT/AST, AFP, and Bil.

Methods: Eligibility criteria were similar for the 2 trials. Pts had advanced HCC, Child-Pugh class A, ECOG PS 0-2, and no prior systemic therapy for HCC. Pts were randomized to Sor 400 mg bid or placebo (Pla) at a 1:1 (SHARP) or 2:1 (AP) ratio. Endpoints included overall survival (OS), disease-control rate (DCR; defined as complete/partial response or stable disease by RECIST maintained for ≥28 days from first demonstration of response), time to progression (TTP), and safety. Pts were grouped by BL levels of ALT/AST, AFP, and Bil. Bil was measured at BL and day 1 of each cycle.

Results: OS and DCR are shown below. No notable differences in safety profiles were observed between Pts with normal vs elevated AFP or Bil levels or not significantly elevated vs mildly/moderately elevated ALT/AST levels. Median BL levels of Bil in the Sor and Pla groups were similar across cohorts for each study. No consistent differences in Bil levels were observed between the Sor and Pla groups by cycle in either trial. Median increases in Bil at last cycle were similar in the Sor and Pla groups for both studies.

Conclusions: Pts with elevated BL levels of AFP or Bil or mildly/moderately elevated ALT/AST had shorter OS than those with normal AFP or Bil levels or not significantly elevated levels of ALT/AST, regardless of treatment. However, the results of our subset analyses suggest that Sor is a safe and effective treatment for HCC, irrespective of ALT/AST, AFP, or Bil levels, and that hepatic function (Bil levels) is not affected by Sor.

Population	n		OS (Sor/Pla)		DCR (%) (Sor/Pla)
	Sor	Pla	Median (mo)	HR (95% CI)	
Total					
SHARP	299	303	10.7/7.9	0.69 (0.55, 0.87)	43/32
AP	150	76	6.5/4.2	0.68 (0.50, 0.93)	35/16
Not significantly elevated ALT/AST (<1.8 × ULN)					
SHARP	152	153	11.6/8.8	0.68 (0.49, 0.93)	53/39
AP	86	46	8.2/8.0	0.76 (0.50, 1.16)	40/22
Mildly elevated ALT/AST (1.8-3.0 × ULN)					
SHARP	77	78	9.5/8.5	0.81 (0.53, 1.24)	36/28
AP	33	18	4.9/3.1	0.57 (0.31, 1.08)	33/11
Moderately elevated ALT/AST* (>3.0 - 5.0 × ULN)					
SHARP	68	72	6.3/4.6	0.71 (0.46, 1.09)	32/21
AP	30	10	4.7/2.0	0.34 (0.15, 0.75)	27/0
Normal AFP (≤ULN)					
SHARP	111	97	12.4/9.5	0.76 (0.51, 1.13)	48/41
AP	26	17	9.2/4.7	0.80 (0.37, 1.72)	46/29
Elevated AFP (>ULN)					
SHARP	171	194	9.4/7.0	0.72 (0.55, 0.95)	40/26
AP	116	59	6.1/4.1	0.64 (0.45, 0.90)	35/12
Normal bilirubin (≤ULN)					
SHARP	225	226	11.1/9.1	0.70 (0.54, 0.91)	49/34
AP	103	47	7.2/4.3	0.68 (0.46, 1.01)	37/15
Elevated bilirubin (>ULN and ≤3.0 mg/dL)					
SHARP	72	77	6.2/5.0	0.77 (0.51, 1.15)	28/25
AP	47	29	5.2/3.9	0.70 (0.42, 1.17)	32/17

ULN=upper limit of normal. *3 Pts in the AP trial had ALT/AST levels >5.0 × ULN, and are not included in this analysis

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751P QUALITY OF LIFE ASSESSMENT WITH COMBINED EORTC QLQ-C30 AND EORTC-HCC18 AS A PROGNOSTIC FACTOR FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA: A PROSPECTIVE STUDY

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Background: For patients (pts) with hepatocellular carcinoma (HCC), patient-reported quality of life (QoL), as measured by EORTC QLQ-C30 (C30), was an independent prognostic factor (Yeo W et al. Ann Oncol. 2006). EORTC QLQ-HCC18 (HCC18) has been derived and suggested to supplement the C-30 in measuring QoL for HCC pts (Blazeby JM et al. Eur J Cancer 2004). There have been no data on combined C30 and HCC18 assessment in HCC. We aimed to investigate the significance of the combined assessment with 2 tools in prognostication of overall survival in HCC pts.

Methodology: Pts with newly diagnosed HCC were recruited prospectively and consented. Pre-treatment QoL assessment was conducted using both C30 and HCC18 scores. By applying multivariate analysis, conventional clinical variables at the time of study entry were analyzed to identify factors that influenced survival. Independent prognostic factors for survival were studied by Cox regression analysis.

Results: Total 203 pts with HCC were recruited. Median follow-up was 14.5 months (ms). Median age=57; 180 M: 23 F. Most (78.8%) had hepatitis B infection. The median survival was 8.1 ms. Multivariate analysis on C30 revealed role functioning and

loss of appetite to be significant prognostic factors, while that on HCC18 showed nutrition scale, fatigue scale and items on sexual interest to be significant. Analyses on combined assessment with C30 and HCC18 found only HCC18 items to be significant. Analyses on the 2 tools and other clinical factors identified high AFP (p< 0.0001; HR= 1.120), bilirubin (p< 0.0001; HR= 1.005), advanced CUPI staging (p< 0.0001; HR= 2.083), curative treatment (p=0.0003; HR=0.236) and worse QoL score in HCC18 fatigue scale (p= 0.0014; HR for 10 point increase=1.124) to be significant.

Conclusions: For pts with HCC, EORTC HCC18 appears to more significant than EORTC-C30 in prognostication. On top of conventional prognostic factors, HCC18 fatigue scale is an independent prognostic factor.

Disclosure: All authors have declared no conflicts of interest.

752P PRELIMINARY PHARMACOKINETICS (PK) AND SAFETY COMPARISON OF CHILD-PUGH A (CPA) VS. CHILD-PUGH B (CPB) PATIENTS (PTS) ENROLLED IN A PHASE 2 STUDY IN HEPATOCELLULAR CARCINOMA (HCC)

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Background: Linifanib (ABT-869) is a novel orally active and selective inhibitor of VEGF and PDGF families of receptor tyrosine kinases. Pharmacokinetic (PK) data indicates that the time to maximum plasma concentration is approximately 3 hr and the elimination half-life is 1 day. The PK appeared dose-proportional between 0.10 mg/kg and 0.30 mg/kg and time-invariant after repeated dosing from Day (D) 1 to 15.

Methods: This phase 2 study is being conducted in Singapore, Taiwan, Hong Kong and North America to determine the efficacy and to establish the safety/tolerability profile of linifanib in pts with advanced hepatocellular carcinoma (HCC). On Study Day (D) 1, after administration of morning dose oral linifanib (0.25 mg/kg), PK samples were collected over 48 hours from 14 pts (9 CPA and 5 CPB). Linifanib exposures (Cmax and AUC) were calculated by non-compartmental analysis using WinNonlin Professional V. 5.2. One pre-dose blood sample was collected on D1 for determination of plasma protein binding to help calculate free exposures. No dose was given on D2, and pts began evening dosing on D3. Linifanib was dosed once daily for CPA pts and every other day for CPB pts, with no food or beverage 2-hrs before and after linifanib dose in a 21-D cycle.

Results: Based on preliminary data from 9 CPA and 5 CPB pts, there appears to be no difference in total and unbound linifanib exposures (measured as Cmax and AUC). Median Tmax was approximately 3 hours for both CPA and CPB pts. Pts with and without hepatic impairment had similar exposures suggesting that no dose adjustment is needed for hepatic impaired pts. The mean number of days on linifanib was 145.5 (range, 4-420+) and 50.5 (range, 11-111) in CPA and CPB pts, respectively. Linifanib-related adverse events (AEs) occurred in all 38 CPA pts (100%) and 6 CPB pts (100%). Linifanib-related serious AEs occurred in 13 of 38 CPA pts (34.2%) and 3 of 6 CPB pts (50%).

Conclusion: The presence of hepatic impairment or its extent in cancer pts (CPA vs. CPB), does not influence Linifanib PK.

Disclosure: N. Gupta, Y. Chiu, M. McKee, J.L. Ricker, D.M. Carlson and R. Pradhan: a full time employee and a stock owner of Abbott. All other authors have declared no conflicts of interest.

753P EFFICACY AND TOLERABILITY OF BEVACIZUMAB (B) AND ERLOTINIB (E) AS FIRST-LINE THERAPY IN ASIAN PATIENTS (PTS) WITH ADVANCED HEPATOCELLULAR CARCINOMA (HCC): A PHASE II TRIAL

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Background: Asian pts with advanced HCC have a poor prognosis and a median OS of 2–4 months with best supportive care (Hsu et al., 2010). Although sorafenib has demonstrated improved median OS of 6.5 months (Cheng et al., 2009), there is still a substantial unmet medical need. Dual inhibition of VEGF and EGFR with B+E is an attractive strategy in HCC. Encouraging efficacy was reported with B+E in a Western population (Thomas et al., 2009). This trial was initiated to investigate the safety and efficacy of B+E in Asian pts.

Methods: Pts with advanced HCC received B 5mg/kg q2w i.v. and E 150mg/day p.o. as first-line therapy. Screening esophagogastroduodenoscopy (EGD) was used to exclude pts with high risk of variceal bleeding. The primary endpoint was PFS at 16 weeks, with response assessed by RECIST. Other endpoints were OS, overall response rate (ORR), disease control rate (DCR) and safety. Pre-treatment tissue samples were collected.

Results: Fifty-one pts were enrolled. Baseline characteristics were as follows: median age 58 years (range 26–84); male/female: 44/7; ECOG performance status 0/1/2: 30/20/1; Child-Pugh A/B: 50/1; BCLC stage C: 44 (88%); hepatitis B/C/B+C/non-B+non-C: 42/4/3/2; grade 1/2 varices: 16 (none with red sign). Forty-three pts (84%) had extrahepatic metastasis and/or major vessel invasion. Nineteen (37%) had prior resection; 25 (49%) received prior trans-arterial chemoembolisation (TACE/TAE) for HCC. Treatment-related toxicities (TRT) were mostly grade 1/2. Grade 3 TRTs in > 1 patient were: rash (n=5), acne (n=5), diarrhoea (n=3), increased transaminases (n=3), hyperbilirubinaemia (n=3), proteinuria (n=2) and GI bleeding (n=2). Only one grade 4 TRT was observed: gastric variceal bleeding, which resolved. PFS at 16 weeks was 35.3% (95% CI 22.4–49.9), median PFS was 2.9 months (95% CI 1.8–4.8) and median OS was 10.7 months (95% CI 7.4–NR). ORR was 6% and DCR was 53%. Among 51 pts, 26 received subsequent systemic therapy: either TKI (11 pts) or chemotherapy (15 pts). Results of biomarker analyses will be reported.

Conclusion: The B+E combination is well tolerated and showed encouraging efficacy in this Asian population.

Disclosure: Y. Kang: I have taken part in advisory boards for Roche, Bayer, Pfizer. T. Chiou: Advisory boards for: GSK, ITP and CLL, Novartis Taiwan-CML Corporate sponsored research: Pfizer Taiwan and GSK. K. Jin: Full time employee of Roche Australia. All other authors have declared no conflicts of interest.

754P MANAGEMENT AND CANCER OUTCOMES OF SECONDARY MALIGNANCIES FOLLOWING LIVER TRANSPLANTATION

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Background: Transplant recipients are at high risk for development of malignancy. Data from renal transplantation recipients shows almost 40% of long term survivors developing cancer. Malignancies in the post transplant population prove a significant management challenge for oncologists due to the difficulty of balancing preservation of the transplanted organ, the toxicities and side effect profile of the immunosuppressant agents used, and the possible interactions between chemotherapeutic agents and the immunosuppressants. To date there are no guidelines for of solid organ malignancies in transplant recipients. We have reviewed the management and cancer outcomes of patients who develop malignancy post liver transplantation in order to identify key management challenges in this setting.

Methods: This was a single centre retrospective audit. The liver transplant unit database was used to identify patients who had developed malignancy. The database was also cross checked against the Cancer Registry to ensure all patients were identified. The medical records and investigation results of patients identified as having developed secondary malignancies were reviewed. Descriptive analysis of this information was then performed.

Results: Post transplantation malignancies were common. Of the 200 transplant recipients followed through from 1992 to May 2010, 53 patients were identified. The most frequent cancers were squamous cell and basal cell carcinoma of the skin. Other malignancies included hepatocellular carcinoma, prostate cancer, adenocarcinoma of the bowel and lymphoma. There was variation in the management of the immunosuppressive regimen following diagnosis of malignancy. There was a significant rate of chemotherapy related toxicity amongst the group who received chemotherapy. Detailed analysis will be included at the time of presentation.

Conclusion: post transplantation malignancies have been shown to present a significant challenge in terms of management. Further prospective studies are required to enable guidelines development for management of these malignancies.

Disclosure: All authors have declared no conflicts of interest.

755P SECOND-LINE CHEMOTHERAPY WITH FLUOROURACIL, LEUCOVORIN, AND IRINOTECAN (FOLFIRI REGIMEN) IN PATIENTS WITH ADVANCED SMALL BOWEL ADENOCARCINOMA AFTER FAILURE OF FIRST-LINE PLATINUM-BASED CHEMOTHERAPY: A MULTICENTER AGEO STUDY

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Background: Small bowel adenocarcinoma (SBA) is a rare tumor with poor prognosis. First-line platinum-based chemotherapy is active in patients with advanced SBA but data regarding second-line chemotherapy are lacking. The aim of this study was to evaluate the efficacy and tolerability of fluorouracil, leucovorin, and irinotecan (FOLFIRI regimen) as second-line chemotherapy in patients with advanced SBA.

Methods: We analyzed all consecutive patients who received second-line chemotherapy with FOLFIRI among 93 patients with advanced SBA included from 1996 to 2008 in a previous retrospective, multicenter study. Progression-free survival (PFS) and overall survival (OS) were estimated from the start of second-line chemotherapy using Kaplan-Meier method. Cox models were applied for multivariate analyses.

Results: Among 51 patients who received second-line chemotherapy, 28 patients (male, 57%; median age, 54 years; metastatic disease, 96%) were treated with FOLFIRI after progression (n=24) or limiting toxicity (n=4) to first-line FOLFOX (n=19) or LV5FU2-cisplatin (n=9). Grade 3-4 toxicity was observed in 48% of patients (grade 3-4 neutropenia, 37%). After a median follow-up of 21.5 months, all patients had tumor progression and 22 patients died. Objective response rate was 20% and disease control rate was 52%. Median PFS and OS were 3.2 and 10.5 months, respectively. No clinical, biological or tumor characteristics were associated with PFS or OS by multivariate analysis. **Conclusions:** Second-line chemotherapy with FOLFIRI produced disease control in half of patients with advanced SBA after failure with first-line platinum-based chemotherapy. Nevertheless, the short median PFS warrants the evaluation of other treatments including targeted therapies.

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756P ALCOHOL, TOBACCO, AND RISK OF GASTROINTESTINAL (GI) CANCERS

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Background: Observational evidence indicates associations of heavy drinking and smoking with several GI cancer types, but relations of alcohol to gastric and pancreatic cancer remain unclear.

Methods: We studied risk of incident invasive gastrointestinal (GI) cancers in a multi-ethnic cohort of 126,293 members of a California comprehensive health care plan. These persons supplied baseline data at routine health examinations from 1978-1985 and were followed through 2008 for GI cancer diagnoses. We used Cox proportional hazards models with 8 covariates (age, sex, ethnicity, education, body mass index, marital status, smoking and usual alcohol intake). Cigarette smoking and alcohol drinking were studied with lifelong abstainers as referent. Cancer site endpoints were: upper airway digestive (UAD) (n = 297), esophagus (n = 113), stomach (n = 285), liver (n = 169), pancreas (n = 470), and colorectum (n = 1,829). These models yielded relative risks (RR), 95% confidence intervals (CI), and p values.

Results: Analyses showed the expected increased risk in relation to smoking for cancers of the UAD, esophagus, and pancreas and the expected increased risk related to alcohol drinking for cancers of the UAD, esophagus and liver (all p values < 0.001). Smoking 1+ packs per day was also related to cancer of the stomach: RR (CI) vs. never smokers = 2.3 (1.6-3.2) and liver: RR = 2.1(1.3-3.6), but was unrelated to colorectal cancer: RR =1.1 (0.9-1.3). Only heavy alcohol intake was weakly related to colorectal cancer; e.g., vs. never drinkers RR for 1-2 drinks per day = 1.1 (0.9-1.2, p = 0.3) and for 3+ drinks per day RR = 1.2 (1.0-1.4, p = 0.047). Neither light-moderate (up to 1-2 drinks per day) nor heavier alcohol intake were related to stomach or pancreatic cancer: e.g., RR for 3+ drinks per day =1.0 for each. Analyses stratified by sex showed no major disparities.

Conclusion: 1. Smoking is related to increased risk of all major types of GI cancer except colorectal. 2. Alcohol drinking has only a weak relation to colorectal cancer and none to cancer of the stomach or pancreas.

Disclosure: All authors have declared no conflicts of interest.

757 CAPECITABINE AND CISPLATIN PLUS CONCOMITANT RADIATION THERAPY IN PATIENTS WITH LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS (LA-SCCE)

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Background: Lee and cols. (J Korean Med Sci. 2009) described a high complete response (CR) rate and a favorable overall survival (OS) and progression-free survival (PFS) using definitive chemorradiotherapy with capecitabine and cisplatin in a pilot study including 18 patients with LA-SCCE. The capecitabine/cisplatin doublet plus concomitant radiationtherapy is a non-infusional alternative for the treatment of LA-SCCE. Here, we describe our institutional experience with this combination.

Methods: Twenty-three consecutive patients with unresectable LA-SCCE were accrued between July/2008-July/2009. They received weekly cisplatin at the dose of 30 mg/m2, starting on day 1, for weeks 1-5, and orally capecitabine, 1600 mg/m2, on days 1-5 for weeks 1-5, plus radiation therapy (54Gy, 2,0 Gy/day, 5 days/week) on weeks 1-5. Two additional courses of cisplatin 75 mg/m2 d1 and capecitabine 2000 mg/m2 d1-d14 were delivered. Study endpoints were clinical response (including biopsy and/or endoscopic evaluation) and safety profile.

Results: The mean age was 56 years, 82.6% of cases with stage III disease and 95% had PS 0-1 (ECOG). All, except 4 patients, completed the planned treatment, with therapy being discontinued due to toxicity in 2 cases. Two patients were lost from follow-up. Sixteen patients (69.6%) were evaluable for response. CR, PR/stable disease and progressive disease were documented in 75%, 6.3% and 18.7% of cases, respectively. Median OS for non-CR and CR patients were 7.5 and 17 months, respectively (p=0,01). All patients were evaluable for toxicity, with severe (grade 3-4) nausea/vomiting/diarrhea, asthenia and neutropenia being observed in 17.4%, 13% and 8,7%, respectively. One treatment related death was documented (4.4%).

Conclusions: Our results confirm previous observations that concurrent chemoradiotherapy with capecitabine and cisplatin is a well-tolerated and highly active regimen for the treatment of patients with LA-ESCC. Prospective randomized trials are needed to evaluate the role of capecitabine compared to 5-FU in the above combination.

Disclosure: J. Brollo: Education grants: Roche. R. Weschenfelder: Research grants: Roche Speaker: Roche Education grants: Roche. All other authors have declared no conflicts of interest.

758 PHASE II STUDY OF DOCETAXEL AND 5-FLUOROURACIL (5-FU) WITH CONCURRENT RADIOTHERAPY IN PATIENTS WITH ADVANCED ESOPHAGEAL CANCER

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Background: Although cisplatin plus 5-FU-based chemoradiotherapy is the most frequently used program in esophageal cancer treatment, it has limited efficacy. We have performed phase I study, combining weekly administration of docetaxel and continuous infusion of 5-FU with concomitant radiotherapy for locally advanced esophageal cancer (Anticancer Res 27:2597,2007). We subsequently conducted phase II study according to the recommended dose (7.5mg/m^2) of docetaxel in phase I study.

Methods: Patients (Pts) with locally advanced esophageal cancer who have adequate organ function were eligible. Pts with distant lesions extending beyond the radiation field were not eligible for this phase II study. During chemoradiotherapy, docetaxel were given at a dose of 7.5mg/m^2 at D1, D8, D22, D29, D43, D50. 5-FU 250mg/m^2/day was administered by continuous infusion for 24 h on the same day of radiation (5 days /week). A toal dose of 60 to 66 Gy was delivered in 2 Gy per fraction.

Results: 26 pts (7 pts in phase I and 19 in phase II) were enrolled and all pts were eligible. In phase II study, the median age was 63 (range 44-79); male/female: 15/4; PS 0/1: 16/3; histology: SCC 19 (100%); tumor location cervical/thoracic: 5/14; UICC (6th ed.)-stage III/IV/IVa/IVb: 13/2/2/2. Complete response was achieved in 6 pts (31.6%), partial response in 11 (57.9%), and 2 pts had progressive disease (10.5%). Over the CTC grade 2 hematological toxicities were not seen. The most common non-hematologic toxicity was esophagitis. Grade 3 or 4 of esophagitis has been developed in 5 pts (26.3%). 11 pts experienced recurrent disease, MST was 18 months and 3-year overall survival was 42.1%.

Conclusions: Concurrent chemoradiotherapy with docetaxel and 5-FU was well tolerated and promising for pts with locally advanced esophageal cancer.

Disclosure: All authors have declared no conflicts of interest.

759 SQUAMOUS CELL CARCINOMA (SCC) OF THE OESOPHAGUS: INDUCTION CISPLATIN-PACLITAXEL-5FU (PTF) BEFORE DEFINITIVE LOCAL THERAPY FOR LOCALLY ADVANCED DISEASE

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Objectives: Induction chemotherapy for locally advanced oesophageal SCC is a subject of intense debate. Triple combination chemotherapy is under study with promising results. We analyse induction therapy with PTF before local definitive therapy in terms of response, resectability, toxicity and survival.

Material and methods: Patients (pts) diagnosed of locally advanced oesophageal SCC have been included. Treatment schedule: Paclitaxel 175 mg/m2 and CDDP 75 mg/m2 on day 1 and 5FU 800 mg/m2/day days 1-4, every 28 days. After 2-3 cycles surgery is considered. If unresectable, radical Radiotherapy (64 Gy) and concomitant Carboplatin (60 mg/m2, d 1 – 5 during first, fourth and, if feasible, seventh week of RT) are administered.

Results: From May-02 to February-10 48 pts have been treated (44 men, 4 women). Age: 56,72 (32 – 70). PS 0-1: 8-40. Location: Upper: 14, Middle: 25, Distal: 8, Whole: 1. T2/3/4:1/26/21, N0/1:12/36. M1a: 6. Weight loss over 10 kg: 11 pts. Cycles delivered: 140. Range: 2-4. Mean 2,91. Median 3. Toxicity (episodes): Anemia 3: 1 episode. Emesis 3: 2. Mucositis 3: 2. Asthenia 2/3: 8. One reactivation of viral hepatitis was reported. Two pts died in remission (one of them with a pathological complete response at necropsy) due to gastrostomy complications and oesophagus-tracheal fistula, treatment related. Two pts developed oesophagus-tracheal fistula as a late event after response to therapy. Response rates: CR 7 (14.6%), PR 16 (33.3%), SD 18 (37.5%), PD 7 (14.6%). Treatment after PTF: Surgery 14 pts (1 upper, 9 middle, 4 distal). One (distal) unresectable at surgery, one (middle) not resected because of liver cirrhosis, two not resected because of liver metastases, unexpected findings at surgery. pCR: 2. pPR 8 (R0: 7, R1: 1) Chemoradiation with concomitant Carboplatin: 25, improving 2 SD to PR, 4 PR to CR and 3 SD to CR. One PR and 4 SD progressed immediately after chemoradiation. Progression: 33 (local 14, systemic 11, both 8). Died: 34 (31 of disease, 2 of complications of gastrostomy, 1 unrelated) Median progression free survival: 35,71 weeks (95% CI 30,21 - 41,20). Median overall survival: 50,71 weeks (95% CI 35,28 - 66,14).

Conclusion: Induction PTF has a good toxicity profile with response rates of almost 50% and disease control over 80% during therapy. Surgical rescue is possible in a good percentage of middle and distal tumours. Local definitive therapy with chemoradiation is the best approach for unresectable or upper third tumours Considering stage at diagnosis, survival curves are promising.

Disclosure: All authors have declared no conflicts of interest.

760 HIGH DOSE BRACHYTHERAPY IN PATIENTS WITH RECURRENT OESOPHAGEAL CANCER AS A PALLIATIVE INTERVENTION

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Introduction: Dysphagia is the commonest and most distressing symptom of relapsed oesophageal cancer and has a major impact on quality of life. High-Dose intraluminal brachytherapy is a suitable alternative to stent insertion and might provide additional survival benefit with a better quality of life according to a metanalysis of 2542 patients from 40 studies by the Cochrane Systemic Reviews.[1]

Patients and methods: We performed a retrospective study of 13 patients with heavily pretreated oesophageal cancer (both adenocarcinoma and squamous cell carcinoma) who developed symptomatic recurrence with dysphagia and were treated with HDR brachytherapy to a dose of 10Gray, prescribed to 1 cm from the midsource or mid-dwell position. The recommended active length is documented on oesophagoscopy at the time of the planned brachytherapy and is the visible tumour with a 1 cm proximal and distal margin.[2]

Results: The symptomatic response rate was 85%. Treatment was well tolerated with few side-effects: acute dysphagia (16%), fatigue (16%) and pain (8%). The median duration of symptomatic response was 5 months. The median survival of patients following brachytherapy treatment was 9 months with 35% surviving longer than 12 months. Following brachytherapy stent insertion was required for 35 % of patients with a median time to stenting of 3.5 months. One patient underwent retreatment with brachytherapy successfully.

Conclusion: Palliative High Dose Rate Brachytherapy is an effective and well tolerated treatment for the dysphagia of recurrent oesophageal cancer. Brachytherapy improves quality of life and could potentially have an impact on survival. More studies need to be performed to identify biomarkers of response to brachytherapy that could lead to better patient selection.

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761 ESOPHAGEAL CANCER IN NORTHEAST OF IRAN

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Background: Esophageal cancer is the 5th most common cancer in Iran. Northern part of the country shows the highest incidence of this malignancy.In this study from north eastern part of Iran, we present some epidemiologic and clinicopathologic characteristics of patients with esophageal carcinoma.

Materials and methods: A cohort of 238 Esophageal cancer patients enrolled in a prospective study of neoadjuvant chemoradiation protocol in a 4 years period (2006-2009). At the admission in oncology clinic their epidemiologic characteristics and clinicopathologic finding registered in a preplanned file. Data consisted of age, sex, race, occupation, residential site, smoking and addiction history sign and symptoms, blood biochemistry profile, imaging and endoscopic finding, etc.The data were analyzed with SPSS software.

Finding: The median age of our patients was 59 years and 55% of them were female. Most of them had Fars (63%) and turkman (13%) races. Seventy two percent were residents of rural areas, 20% were smokers and 22.3% were addicted to opium and its analogues. Only 1.3% of patients were alcohol drinker. Most common presenting symptoms was dysphagia(93.7%), and mostly had grade III dysphagia(46.9%).Location of the tumor in the Esophagus was in the middle third in 53% of patients and lower third in45%. Sixty five percent of the patients had abnormal esophagogram. On endoscopic evaluation the most common types of tumors were polypoid, vegetative and fungoid respectively. Mean lengths of tumor was 5.7 cm. The most common histologic type was squamus cell carcinoma (99.2%) and 51.3% of these patients had moderately differentiated carcinoma. We couldn't find any significant relationship between grade of dysphagia with macroscopic type and pathologic grade of tumor in this study.

Conclusion: Squamus cell carcinoma comprise more than 99% of all esophageal cancers in our patients and this histologic type is the prominent type in northeast of Iran. Middle third is the major site of the cancer in esophagus and unfortunately most of the patients present with grade III dysphasia which reflect advanced stage of disease.

Disclosure: All authors have declared no conflicts of interest.

762 LOW SERUM CHOLESTEROL AS A RISK FACTOR FOR FISTULA FORMATION AND A PROGNOSTIC FACTOR IN T4 ESOPHAGEAL CANCER PATIENTS WITH DEFINITIVE CHEMORADIOTHERAPY

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Background: Definitive chemoradiotherapy (CRT) is a standard treatment for esophageal cancer invading adjacent organs (T4) without distant metastases. Definitive CRT for T4 esophageal cancer has a curative potential but often induces severe adverse events including fistula formation. The aim of this study was to investigate prognostic factors and risk factors for DCRT-related fistula formation in T4 esophageal cancer.

Method: We retrospectively analyzed the characteristics of consecutive 90 patients with T4 esophageal cancer treated by 5FU, cisptlatin and concurrent radiation of 60Gy (2Gy/day, 30 fractions) in our institution between Sep 2002 and Apr 2009. We evaluated the efficacy of CRT, the frequency and risk factors of CRT-related fistula formation without tumor progression and prognostic factors.

Results: The median age of patients was 65 year, 84 of them were male (93%). 89 (99%) of patients have histopathologicaly proven squamous cell carcinoma. The median length of tumor was 7.3cm. Clinically involved sites were as follows; aorta (n=45), trecheobronchial tree (n=56), pericardium (n=23), others (n=9). The median survival time was 13.4 months with a median follow-up period of 29.8 months. Two-year and 3-year survival rates were 34%, 28%, respectively. CRT-related fistula formation was observed in 15 patients (17%). CRT-related death occurred in 8 patients (9%), due to aorto-esophageal fistula in five. By univariate analysis in 86 patients without fistula before CRT, clinical invasion to aorta (OR 6.03, 95%CI 1.15-31.7, P=0.033) and low serum cholesterol (OR 5.15, 95%CI 1.69-5.04, P=0.015) were identified as independent risk factors of fistula formation. Tumor size (>8cm), hemoglobin (<13g/dl), cholesterol (<170mg/dl), albumin (<3.5g/dl) and CRP (>1.0mg/dl) were associated with poor prognosis. In multivariate analysis using Cox proportional hazard model, low serum cholesterol at pretreatment was also independent poor prognostic factor (HR 2.92, 95%CI 1.69-5.04, P=0.015).

Conclusion: Low serum cholesterol might be a risk factor for fistula formation and poor prognostic factor in T4 esophageal cancer patients with definitive CRT.

Disclosure: All authors have declared no conflicts of interest.

763 TREATMENT OUTCOME OF DOCETAXEL AS SALVAGE CHEMOTHERAPY IN ADVANCED GASTRIC CANCER AFTER FAILURE OF OXALIPLATIN (FOLFOX) AND IRINOTECAN (FOLFIRI) BASED SEQUENTIAL CHEMOTHERAPY

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Purpose: We performed multicenter retrospective study to evaluate the activity and the safety of a docetaxel as salvage chemotherapy in advanced gastric cancer patients who had undergone oxaliplatin (FOLFOX) and irinotecan (FOLFIRI) based sequential chemotherapy regimens.

Methods: Thirty-eight patients with advanced gastric cancer previously treated were eligible for this study. Patients received docetaxel 30mg/m^2 +/- cisplatin 30mg/m2 IV on day 1, 8 or docetaxel 60mg/m^2 +/- cisplatin 60mg/m2 IV on day 1 every 3 weeks until disease progression, and responses were assessed after every two cycles according to RECIST criteria and toxicity was evaluated by NCI-CTC (version 3.0).

Results: Thirty-two out of 38 patients were evaluable for response. A total of 95.1 cycles of chemotherapy (median 2, range 0.5–7) were administered. Relative dose intensities of docetaxel and cisplatin were 93.4% and 87.8%, respectively. The overall response rate was 15.6% and the disease control rate was 50%. With a median follow-up duration of 3.1 months (range 0.3-14.3 months), 36 patients had disease progression, and 34 patients had died at the time of analysis. The median progression-free survival (PFS) was 1.8 months (95% CI, 1.3–2.3 months). The median overall survival (OS) was 3.1 months (95% CI, 2.3–3.9 months). Good performance status (ECOG 0-1) in patients was predictive of longr PFS and OS. Bone mtastasis wih patients were predictive of shorter OS. Grade 3 or 4 hematologic toxicities included neutropenia in thirteen patients (38.3%), febrile neutropenia in four patients (11.7%). and thrombocytopenia in one patient (2.9%). Other grade 3 or 4 toxicities included neuropathy in three patients (8.8%) and mucositis in two patients (5.9%). There were three treatment-related deaths (8.8%) caused by infection associated with neutropenia.

Conclusion: Salvage docetaxel chemotherapy in AGC patients failed in oxaliplatin and irinotecan based treatment is not recommend routinely. However, selected patients with good performance status may have derived some survival benefits from salvage chemotherapy.

Disclosure: All authors have declared no conflicts of interest.

764 A PHASE II STUDY WITH CAPECITABINE AND CISPLATIN AS FIRST-LINE THERAPY IN ADVANCED GASTRIC CANCER

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Background: Nowadays, randomized phase III studies' results show marginal differences concerning the survival rate in first-line therapy in advanced gastric cancer (AGC) and do not strongly support the use of a specific protocol as standard treatment. Objectives: evaluate the efficiency (global response rate, time to progression, overall survival) and safety of the low-doses of XC (Capecitabine + Cisplatin).

Patients and methods: 42 patients (pts) with histopatologically confirmed evaluable AGC who had not underwent previously chemotherapy, more than 18 years old and with Karnosky (PSK) [3] 60% were treated with Capecitabine (X) 850 mg/m2 b.i.d. for 14 days and Cisplatin (C) 70 mg/m2 iv day 1 every 3 weeks until disease progression. The recommended low-doses for this phase II study were obtained in our previously phase I trial.

Results: Between June 2005 and June 2009, 42 pts (32 male/10 female) were treated with the previous protocol. The median age was 62 years (range, 39-79) and 14 pts (33%) had more than 65. Median KPS: 70%. Number of metastatic sites: 1, 21 pts, 2, 15 pts and 3 or more, 6 pts. Involved metastatic organs: nodes (n=25), liver (n=19), peritoneum (n=15), lung (n=8), others (n=6). The median of the cycles of chemotherapy that pts received was 6 (range, 1–12). Efficiency: 1 patient with complete response (2.86%) and 14 pts with partial response (40%), ORR of 42.86% (95% CI 26.46–59.25%). Median time to progression was 5 months (95% CI 4-7 months) and overall survival rate was 11 months (95% CI 10-14 months). Tolerance: 2 pts with grade 4 toxicity. Grade 2-4 toxicity: vomiting 62%, neutropenia 40%, hand-foot syndrome 36%, mucositis 24%, alopecia 22%, anemia 19%, neuropathy 12%, diarrhea 7% and nefrotoxicity 6%. 16 pts (38%) underwent surgery for primary tumour, 27 pts (65%) received second-line chemotherapy (docetaxel) and 7 pts (17%) received a third-line treatment (irinotecan +- bevacizumab).

Conclusions: The XC' doses used in the study showed not only an efficiency and a survival rate comparable with the high ones (Kang YK, Ann Oncol 2009;20(4):666-73) but also minor and more manageable toxicity fact that could make them a better option as first-line treatment in AGC if the results are confirmed by phase III studies.

Disclosure: All authors have declared no conflicts of interest.

765 COMPARISON OF CFF (CISPLATIN, 5-FLUOROURACIL, FOLINIC ACID) AND MODIFIED DCF (DOCETAXEL, CISPLATIN, 5-FLUOROURACIL) REGIMENS IN THE FIRST LINE TREATMENT OF METASTATIC GASTRIC CANCER

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Aim: We aimed to compare the efficacy and the toxicity of CFF versus modified DCF regimen in the first line treatment of metastatic gastric cancer, retrospectively.

Patients and methods: Between June 2004 and October 2008, 30 patients were administrated CFF (cisplatin 50 mg/m^2 d1, folinic acid 200 mg/ m^2 d1, 5-FU 400 mg/ m^2 d1 iv bolus and 1600 mg/ m^2 46-hours infusion every 2 weeks), and 40 patients were administrated mDCF (docetaxel 60 mg/m^2 d1, cisplatin 60 mg/ m^2 d1, 5-FU 600 mg/ m^2/day d1-5 every 3 weeks). None of the patients were given colony stimulating factors as primary prophylaxis. None of the patients were given colony stimulating factors as primary prophylaxis. The survival and toxicity were compared.

Results: The median age of patients was 53 (23-69) years. Forty eight of the patients were male and most of them (75.7%) had ECOG performance status (PS) of 0-1. No significant differences in the prognostic factors (age, ECOG PS, histopathological grade and the number of metastatic regions) were found between two groups. The objective response rates (complete + partial response) were higher in the mDCF group (13.3% vs 30.0%, p=0.19). The median follow up period was 10.3 (1.5-59.6) months. Ninty per cent of the patients in CFF and 97.5% of the patients in mDCF groups died. The median time to progression was 4.4 months (95% CI: 1.8-7.0) for CFF group and 6.2 months (95% CI: 5.6-6.8) for mDCF group (p=0.85). The median overall survival was 6.5 months (95% CI: 1.8-11.2) for CFF group and 8.7 months (95% CI: 6.7-10.7) for mDCF group (p=0.88). Toxicity was acceptable in both groups. The most commonly observed grade 3-4 toxicities were anemia 3.3% and 5.0%, neutropenia 20% and 7.5%, febrile neutropenia 6.7% and 5.0%, diarrhea 3.3 % and 5.0% in CFF and mDCF groups respectively.

Conclusion: Although statistically insignificant, mDCF was found to have a trend of superiority in regard to disease-free and overall survival and has an acceptable toxicity profile as compared to CFF in the first line treatment of metastatic gastric cancer.

Disclosure: All authors have declared no conflicts of interest.

766 MANAGEMENT OF ADVANCED GASTRIC CANCER USING CAPECITABINE IN KORLE BU TEACHING HOSPITAL, GHANA: AN EXPERIENCE FROM A RESOURCE LIMITED SETTING

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Background: The use of Capecitabine (X) in place of 5 Fluorouracil (5FU) for the management of gastrointestinal tumors has shown comparable results. For gastric cancer, Capecitabine has been combined with Platinums and Anthracyclines as neoadjuvant treatment or with radiation as adjuvant treatment. Rationale for using Capecitabine in Ghana is the lack of skilled staff and logistics for continuous infusion 5FU. This retrospective study reviews the outcome of advanced gastric cancer patients treated at the Oncology Unit of Korle Bu Teaching Hospital, Ghana from 2004 to 2008.

Patients and methods: Medical records of 27 patients with biopsy proven gastric cancer were analyzed for age, stage, treatment received, toxicity and time to progression (TTP)

Results: Median follow up was 12 months (1 to 60 months). 53.6% presented with locally advanced disease, 42.9% had metastatic disease and 1 patient had local recurrence. 20 patients (74%) had surgery; partial gastrectomy in 80% and palliative gastrojejunostomy in 20%. 9 patients had lymphadenectomy done. 1 patient had neoadjuvant chemotherapy with Epirubicin (E), Cisplatin (C) and 5FU for one cycle and XC for two cycles. 26%of patients had adjuvant radiotherapy 44 t0 46Gy at 1.8 to 2Gy/ fraction with concurrent Capecitabine 825mg/m^2 bid. 3 patients received palliative radiotherapy as 30Gy in 10 fractions. One patient did not complete radiotherapy due to side effects. Capecitabine only was given to 3 patients (11.1%) for palliation. Adjuvant chemotherapy was given as Capecitabine only 1000mg/m^2 bid day 1 to 14 in 4 patients (14.8%) and with Oxaliplatin 130mg/m^2 on day 1 in 3 patients (11.1%). One patient received Cisplatin 60mg/m^2 and Adriamycin. Grade 3/4 diarrhoea was reported in 2 patients (7.4 %); neuropathy and neutropenia were seen in one patient each, necessitating dose reductions. All patients however completed adjuvant chemotherapy. Median TTP after adjuvant treatment was 6.4 months (2 to 13 months)

Conclusion: Capecitabine is tolerable when given alone or combined with other chemotherapy or radiation. This tolerability ensured good compliance to treatment. Capecitabie compares favorably with 5FU for advanced gastric cancer.

Disclosure: All authors have declared no conflicts of interest.

767 EXPERIENCE OF CHEMOTHERAPY WITH MODIFIED FOLFOX AS FIRST-LINE IN ELDERLY BANGLADESHI PATIENTS POPULATION WITH ADVANCED GASTRIC CANCER

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Background: In Bangladesh usually patients report to oncologists in advanced stages. In case of gastric cancer the fact is almost regular phenomenon. Patients general conditions and performance status usually not in favour of conventional chemotherapy with cisplatin and taxane. So, we had conducted a phase II study to evaluate the efficacy and safety of biweekly oxaliplatin in combination with continuous infusional 5-fluorouracil and leucovorin (modified FOLFOX regimen) in Bangladeshi elderly patients with advanced gastric cancer (AGC).

Methods: Thirty-five eligible patients older than 65 years with previously untreated AGC received oxaliplatin 85 mg/m^2 intravenously over a 2-h period on day 1, together with leucovorin 400 mg/m^2 over 2 h, followed by a 46-h infusion of 5-fluorouracil 2600 mg/m^2 every 2 weeks. All patients were evaluable for efficacy and toxicity. A median of six cycles (range 3-12) was administered. It was a multi-centric prospective non-randomized study. Performance status of the patient was

Results: The overall response rate was 48.6% [95% confidence interval (CI): 31-61%] with two complete responses, 16 partial responses, 9 stable diseases, and 8 progressions. Median time to progression was 6.7 months (95% CI: 4.6-7.8) and median overall survival was 10.2 months (95% CI: 8.9-11.8). Toxicity was fairly mild. Grade 3 toxicities included neutropenia (9.7%), nausea (5.3%), vomiting (3.3%), diarrhea (3.2%); and grade 4 toxicities occurred in none of the patients. Grades 1-2 peripheral neuropathy was reported in 41.5% of patients.

Conclusions: The modified FOLFOX regimen is active, well tolerated as first-line chemotherapy for elderly Bangladeshi patients aged above 65 years with AGC.

Disclosure: All authors have declared no conflicts of interest.

768 FEASIBILITY OF SURGERY FOLLOWED BY CHEMORADIOTHERAPY IN GASTRIC CANCER. PHASE II TRIAL

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In gastric cancer, efficacy of postoperative chemoradiotherapy (CRT) has been demonstrated. However, the feasibility of the whole treatment with surgery followed by postoperative CRT remains unknown. The aim of the phase II trial was to assess the feasibility of the whole treatment.

Inclusion criteria: histologically proven gastric adenocarcinoma, T3and or N+, M0 according to CTscan, endoscopic ultrasound. Performance status(PS) (grade0,1) allowing major surgery. The treatment was a surgical resection with gastrectomy according the localization of tumor, D1,5 lymphadenectomy, then 60 days after the surgery, chemotherapy by 4 courses of FOLFIRI followed by concomitant CRT consisted of 5FU 200 mg/m2 days 1 to 5 each week of radiotherapy. A total dose of 50 Gy was given (2.0 Gy/fract, 5 fract/w). A complete treatment was defined by surgical resection and full of chemotherapy courses and at least 22.5 fractions of radiotherapy (90% of fractions) and 75% dose of 5FU during the radiotherapy. A feasibility rate of 70% was uninteresting and 88% was expected. Using Fleming two step design (unilateral alpha 5% and power of 90%) it was required 21 patients at the first step and to observe 17 to 20 patients achieving treatment feasibility to pursue inclusion of 21 patients in 2nd step.

Results: Between 11/07 and 06/09, 21 patients (pts) were included in 10 centers. Mean age was 61.7 (range: 39.2-77.7). Mean serum albumin was 38.6 g/l. PS was 0 and 1 in 15 and 6 patients respectively. Surgical exploration, all courses of FOLFIRI and radiotherapy with 50Gy were performed in 21, 12 and 12 pts respectively. The whole treatment was performed in only 9/21 pts (42.9% CI 95%: 21.7-64.0). A severe adverse event (grade 3-4) was reported in 6 pts (28.6%) during the treatment. Trial was stopped for futilty

Conclusion: Postoperative CRT cannot challenge the gold standard defined by perioperative chemotherapy.

Disclosure: All authors have declared no conflicts of interest.

769 GASTRIC CANCER (GC) ADJUVANT (A) CHEMOTHERAPY (CT): A LITERATURE BASED META-ANALYSIS (MA)

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The use of ACT in GC is controversial. We performed a MA of the randomized phase III trials concerning this issue. An electronic (MEDLINE, Cochrane) and manual (ASCO and ESMO proceedings, references of selected articles, published reviews) search has been performed. We retrieved the available data from papers published since 1990, aimed to evaluate the effect of ACT after surgery in terms of 5-yr SR and disease free survival rate (DFSR) (HR, 95% Confidence Interval, CI). To avoid potential biases and possibly select the most effective combination, subgroup analysis (SA) for country (EU, USA, Asia), decade of publication (1990-2009, 2000-2009), regimen (anthracycline vs non-anthracycline; oral vs ev CT), proportion of pts with T3 (≤70% vs >70%), with a lymph-nodes (LN) resection level ≥D2 (≤50% vs >50%), with LN+ (≤70% vs >70%) have been done. A random effects model was used.

We included 18/425 studies (4632 pts, 2374 in the investigational, 2392 in the control arm). The administration of ACT resulted in a significant improvement of both 5-yr SR (HR 0.77, 95% CI 0.71 – 0.85; p<0.05) and DFSR (HR -0.29, 95% CI -0.40 – -0.18). Since the HR, though statistically significant, provides only an estimate of the advantage, the risk difference (RD) for 5-yr SR and DFSR has been evaluated showing ACT is significantly risk-reducing (SR RD -0.07, 95% CI -0.09 – -0.04, p<0.05; DFSR RD -0,08; 95% CI, -0.11 – -0.04, p < 0,05).

In the SA a statistically significant HR was confirmed favouring ACT regardless country (Western 0.81 95% CI 0.73 – 0.90, Asia 0.66 95% CI 0.54 – 0.80; p<0.05), decade of publication (1990-1999 0.76 95% CI 0.66 – 0.88, 2000-2009 0.78 95% CI 0.69 – 0.89; p<0.05), drugs administered (anthracycline 0.85 95% CI 0.76 – 0.95, no-anthracycline 0.64 95% CI 0.54 – 0.76; p<0.05), route of administration (ev 0.83 95% CI 0.74 – 0.92, oral 0.65 95% CI 0.54 – 0.78; p<0.05), proportion of pts with T3 (≤70% 0.76 95% CI 0.66 – 0.88, >70% 0.78 95% CI 0.68 – 0.90; p<0.05), LN resection level ≥D2 (≤50% 0.83 95% CI 0.71 – 0.97, >50% 0.74 95% CI 0.65 – 0.85; p<0.05), LN + (≤70% 0.74 95% CI 0.63 – 0.86, >70% 0.79 95% CI 0.70 – 0.89).

ACT can improve survival for pts radically operated for GC: oral administration of non-anthracycline containing combinations seem to have a superior activity.

Disclosure: All authors have declared no conflicts of interest.

770 EFFICACY AND NECESSITY OF NASOJEJUNAL TUBE AFTER GASTRECTOMY

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Background: In many centers, nasojejunal tube (NJT) is routinely used for gastrointestinal drainage after total gastrectomy. It is supposed that it would protect anastomosis, but since the stomach should be completely removed, today its efficacy is under question. On the other hand, the tube leads to patients discomfort and aspiration disorders or esophaseal ulceration. The aim of this study is to evaluate the efficacy and necessity of nasojejunal tube after gastrectomy.

Methods: In this interventional study, 50 patients who underwent gastrectomy due to gastric cancer in Gheam and Omid hospitals related to Mashhad University of Medical Sciences from 2001 to 2008 were enrolled. The patients were randomly divided into two groups of with NJT (25 cases) and without NJT (25 cases). The rate of complications, infective or non-infective, hospitalization duration and the time of beginning diet were evaluated.

Results: Two groups were similar in age, sex, extend of involvement, bleeding volume and length of removed esophagus. There was no significant difference between two groups in the view of first gas passing, beginning of diet, and hospitalization duration. But incidence of sore throat, nasal discomfort, speech disorders, and patients' unsatisfactory were higher in with NJT group.

Conclusion: It seems that patients without NJT were more comfortable and satisfactory after total gastrectomy. So, there is no need for insertion of NJT after gastrectomy.

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771 NEUTROPENIA AS A PROGNOSTIC FACTOR IN ADVANCED GASTRIC CANCER PATIENTS UNDERGOING SECOND-LINE CHEMOTHERAPY WITH WEEKLY PACLITAXEL

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Background: Neutropenia during chemotherapy has been reported to be a predictor of better survival in patients with several types of cancers, although there are no reports in pretreated patients.

Methods: We retrospectively analyzed 242 patients with advanced gastric cancer who received weekly paclitaxel as second-line. Background characteristics and neutropenia as time-varying covariates were analyzed as prognostic factors.

Results: Of the 242 patients, mild neutropenia (grade 1–2) occurred in 101 patients (41.7%) and severe neutropenia (grade 3–4) occurred in 63 patients (26.0%). The other 78 patients (32.2%) did not experience neutropenia. The median overall survival times in the absent group, mild group, and severe group were 3.9 months (95% CI, 2.7-5.2), 8.8 months (95% CI, 5.9-10.4), and 8.1 months (95% CI, 6.3-10.5), respectively. According to a multivariate Cox model with neutropenia as a time-varying covariate, hazard ratios of death were 0.61 (95% CI, 0.43-0.85; p = 0.004) for patients with mild neutropenia and 0.61 (95% CI, 0.41–0.88; p = 0.009) for those with severe neutropenia. Among the patients in landmark analysis (landmark of 2.5 months; median time to treatment failure of paclitaxel), mild and severe neutropenia remained significant prognostic factors with the HR for mild neutropenia in comparison to absent neutropenia of 0.60 (95% CI, 0.41-0.88; p=0.009), and the HR for severe neutropenia in comparison to absent neutropenia of 0.65 (95% CI, 0.44–0.98; p=0.048).

Conclusion: Our results indicate that neutropenia during chemotherapy is associated with improved survival in patients with advanced gastric cancer who received weekly paclitaxel as second-line chemotherapy. Prospective trials are required to assess whether dosing adjustments based on neutropenia may improve chemotherapy efficacy.

Disclosure: All authors have declared no conflicts of interest.

772 MANAGEMENT OF HEMATOLOGIC TOXICITY IN PATIENTS WITH ADVANCED OR METASTATIC GASTRIC CANCER TREATED WITH DOCETAXEL, CISPLATIN AN FLUOROURACIL (DCF): RESULTS OF MONOCENTRIC EXPERIENCE

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Background: Gastric adenocarcinoma is the second most common cause of cancer death worldwide. There is no standard regimen of chemotherapy for metastatic disease, although the regimen of ECF is the most used regimen, with a median survival of 7-9 months. With new regimens of chemotherapy, such as DCF, the median survival has increased, despite a major toxicities and 1-2% of toxic death.

Patients and methods: From January 2006 until December 2009 we have treated 36 chemo-naïve patients with histological diagnosis of locally advanced or metastatic gastric cancer with a DCF regimen associated with prophilactic Peg-filgrastim treatment at 6th day of therapy.

Results: A total of 168 cycles were administered (median 5 per patient, range 3–8). Major responses were observed in 10 patients, with 2 complete (5,5%) and 8 partial remissions (22,2%); 16 additional pts showed disease stabilization (44,4%) and 10 progressed (27,9%). Median OS times were 12 months. Median TTP were 9,5 months. Toxicity was acceptable, worst per patient toxicities were neutropenia (grade 3-4 in 15%), feverish neutropenia (11,1%) diarrhoea (grade 2 in 25% , grade 3 in 25%, grade 4 in 18,8%), asthenia (grade 2 in 8%), neurotoxicity (grade 3 in 4%),anhemia (grade 4 in 10%), four pts received blood transfusion.

Conclusion: DCF scheme in locally advanced or metastatic gastric carcinoma is one scheme that provides good results both in terms of Time to Progression an Overall Response Rate and that has an acceptable toxicity even in not highly selected patients.

Disclosure: All authors have declared no conflicts of interest.

773 AN ARTIFICIAL NEURAL NETWORK FOR PREDICTING RECURRENCE IN PATIENTS WITH DISTAL GASTRIC ADENOCARCINOMA UNDERWENT GASTRECTOMY

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Background: Surgical treatment of gastric cancer has been universally recognized as the most effective way of treatment. However, even when a curative resection is possible, recurrences are common. At present, it is still impossible to make reliable predictions of recurrence of the tumor. Purpose: The aim of our study was to determine whether artificial neural networks (ANNs) could be used to predict local recurrence following gastrectomy in patients with distal gastric adenocarcinoma.

Methods and materials: A total of 66 patients underwent total (35 patients) or subtotal (31 patients) gastrectomy for early adenocarcinoma of the antrum were included in our prospective nonrandomized controlled trial. The patients were followed up with a mean duration of 77.7 months (ranging from 1 to 85 months). Recurrence was assessed using computed tomography scans and clinical symptoms. For constructing the predictive neural network, the cases were divided into a model development (47 patients) and validation group (19 patients). By using a multilayer perceptron neural network with one hidden layer, patients' variables including age, gender, type of surgery (total or subtotal), length of hospital stay after the surgery, and 5 measures of quality of life (QoL) following surgery were used to predict the local recurrence of the tumor.

Results: The ANN predicted the recurrence with the sensitivity of 93% and specificity of 90%. Positive and negative predictive values were 86% and 95%, respectively. Overall QoL was the best predictive variable with the importance of 0.220 in the model. The ability to work 1 month after surgery was the second most important predictive indicator (importance=0.171).

Conclusions: The results show that artificial neural networks can accurately predict the recurrence of the distal gastric adenocarcinoma in patients underwent surgery. QoL after surgery would be the best predictor of the recurrence.

Disclosure: All authors have declared no conflicts of interest.

774 SERUM LDH LEVEL AS A PROGNOSTIC FACTOR FOR THE PATIENTS WITH ADVANCED GASTRIC CANCER

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Background: Though serum LDH level is frequently elevated in the patients with advanced gastric cancer, its clinical significance is still elusive. Moreover, the relationship between the change of serum LDH level after chemotherapy and the response to the treatment has not been studied, yet. We analyzed serum LDH level as a prognostic factor for the patients with advanced stomach cancer.

Methods: We assessed serum LDH level before chemotherapy for the patients who were planned to receive palliative chemotherapy. We re-assessed their serum LDH level at the time when the response to chemotherapy was evaluated after 2-4 cycles of treatment. The survival duration and the response to chemotherapy for the patients with low serum LDH level were compared to the survival duration and the response to chemotherapy for the patients with high serum LDH level. The relationship between the change of serum LDH level and the response to the treatment was evaluated, too.

Results: Total 118 patients were entered into this study and 114 patients were evaluable for their response to chemotherapy. Pre-treatment serum LDH level was normal in 88 patients and elevated in 30 patients. The response rate in the patients with high serum LDH level was significantly higher than the response rate in the patients with normal serum LDH level (34.5% versus 15.3%, $p < 0.05$). However, the patients with normal serum LDH level lived longer than the patients with high serum LDH level (median: 378 days versus 206 days, $p < 0.001$). The normalizing of the elevated serum LDH level after chemotherapy was related to the good response to treatment (response rate 50.0% versus 18.8%, $p < 0.05$).

Conclusion: For the patients with advanced gastric cancer, high serum LDH level was related to better response to chemotherapy but shorter survival duration. The normalization of elevated serum LDH level after chemotherapy was related to good response to treatment.

Disclosure: All authors have declared no conflicts of interest.

775 PROGNOSTIC SIGNIFICANCE OF S100A4 EXPRESSION IN CURATIVELY RESECTED STAGE IV STOMACH CANCERS

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Background: Stage IV stomach cancers were still incurable disease and have a poor prognosis. However, limited cases of resectable stage IV stomach cancer could be cured and showed long-term survival. S100A4, the S100 family of calcium-binding protein, was known as a metastasis related genes and correlated with cancer invasion and metastasis. We investigate the role of S100A4 expression as a prognostic marker in patients with curatively resected stage IV stomach cancer.

Methods: Archival tissues from patients with curatively resected stage IV gastric cancers who had no macroscopic residual lesion on postoperative imaging study were obtained. The expression of S100A4 was evaluated by immunohistochemistry. The relationships between S100A4 expression and several clinicopathological variables including survival time were analyzed.

Results: Total 62 patients were evaluated and 42 patients(67.7%) were relapsed. The median disease free survival(DFS) and overall survival(OS) of all patients was 15.1 and 24.5 months. The incidence of S100A4 expression was 22.6%(14/62). On survival analysis, the median DFS and OS of S100A4 positive group was shorter than that of S100A4 negative group (DFS 9.3 vs 17.1 months, p=0.082, OS 12.7 vs 27.4 months, p=0.024). The Cox proportional hazard ratio (HR) test identified S100A4 expression (HR, 3.129; 95% confidence interval [95% CI], 1.424–6.873; P = .004) and high positive LN ratio (HR, 5.809; 95% CI, 2.152–15.680; P = .001) as prognostic factors on OS.

Conclusions: The expression of S100A4 is useful in assessing the prognosis of patients with curatively resected stage IV stomach cancers and more aggressive postoperative therapy should be considered for such patients. We suggest that these results could be useful for the development of new target agent to S100A4.

Disclosure: All authors have declared no conflicts of interest.

776 THROMBOEMBOLISM IN PATIENTS WITH ADVANCED GASTRIC CANCER

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Background: The association between thromboembolism (TE) and cancer is well recognized. Thromboembolic events, which includes venous (VTE) and arterial thromboembolism (ATE), also occur commonly in gastric cancer. However, there is a shortage of data on thromboembolism in advanced gastric cancer.

Methods: We reviewed 302 patients with advanced gastric cancer to obtain incidence, risk factors and prognosis of thromboembolism in a single institute.

Results: Of 302 advanced gastric cancer patients, 32 patients (10.6%) diagnosed thromboembolism, including VTE of 25 patients (8.3%), ATE of 9 patients (3.0%). The 2-year cumulative incidences of all TE events were 2.9%, 4.0%, 6.5% and 18.3% in stages I, II, III and IV. Advanced stage, poor performance, no major surgery, poor response to treatment, recurred case, many comorbidities and high platelet level were risk factors for developing TE. However, age, histology and endoscopic findings were not associated with TE. When the VTE cases were classified into extremity venous thrombosis (EVT), pulmonary thromboembolism (PTE) or intra-abdominal venous thrombosis (IVT), IVTs (64%) were most common than EVTs (8%), PTEs (28%). Among the ATE cases, myocardial infarction (MI) (44%), cerebrovascular accident (CVA) (44%) were more common than peripheral arterial disease (11%). ATE was a significant predictor of early death when compared with no occurrence of TE (p=0.267). The patients who diagnosed VTE tend to have shorter survival than the patients without TE. However, this was not statistically significant (p=0.864)

Conclusion: The incidence of TE in AGC patients was comparable with other studies and we observed thromboembolic events more frequently with patients with far advanced stage. ATE was the only significant adverse prognostic factor for survival, but not VTE.

Disclosure: All authors have declared no conflicts of interest.

777 HER2 STATUS IN 100 PATIENTS WITH GASTRIC ADENOCARCINOMA

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Background: HER2 positivity is thought to be a negative prognostic factor in gastric cancer (GC). With the results of a phase III study (ToGA), the benefit of trastuzumab in combination with chemotherapy in HER2-positive metastatic GC has been established. However, few data on HER2 status in GC patients from Latin America are available. The objective of this study is to analyze the pathological features of GC and the relationship with HER2 expression.

Methods: Data were collected prospectively from 100 GC patients from July 2009 to March 2010 from our institution. GC tumor samples were centrally reviewed by immunohistochemistry (IHC) for HER2 expression (HercepTest). A HER2-scoring system modified from the protocol in breast cancer (BC) was used. We defined HER2 positive as IHC 3+ or FISH+. In addition, age, gender, histology, stage and therapy received were also recorded. T and chi-square tests were used for comparison of continuous and categorical variables, respectively. This study was approved by our institution's IRB.

Results: The median age was 70 years with a male-to-female ratio of 1.5:1. No differences in age and sex between the HER2-positive and HER2-negative groups were found. Seventeen cases were located in the gastroesophageal junction (GEJ) and 83 were located in the stomach. Overexpression of HER2 was detected in 9 (9%) of 100 GC patients. Eight patients had IHC3+ and one IHC2+ had FISH+. From the HER2-positive group, all cases were of intestinal type. One case was stage II, five cases stage III and three cases stage IV. The overexpression rate of HER2 in stage III/IV disease was significantly higher than that in stage I/II disease (15% vs. 3%, p=0.045). Five cases (56%) were localized in the GEJ and the other four (44%) were primarily gastric. HER2-positivity rates according to tumor location were higher in GEJ than in GC (33% vs. 5%; p=0.005). Survival data is not yet available.

Conclusions: HER2-positivity in Peruvian patients with metastatic GC displays a similar heterogeneous staining to that reported in the ToGA study. Patients with primary disease in the GEJ had higher rates of HER2-positivity. The HER2 positivity rate was also higher in advanced stages suggesting its late role in GC oncogenesis.

Disclosure: All authors have declared no conflicts of interest.

778 IMMUNOHISTOCHEMICAL EXPRESSION OF HER2 IN LINITIS PLASTICA–TYPE GASTRIC CARCINOMA

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Background: HER2 overexpression in gastric cancer has become an important target of treatment in gastric carcinoma since the TOGA trial's results. In this study as in some other, HER2 expression was highly correlated with histologic subtype, reported as significantly higher in intestinal than diffuse type. The aim of our study was to evaluate the frequency of HER2 expression in a homogeneous group of diffuse, linitis plastica gastric carcinoma (LPGC) and to report clinico-pathological characteristics, treatment regimen, prognosis factor and survival rates.

Patients and method: 305 cases of patients with gastric carcinomas consecutively treated between 2003 and 2009 were reviewed. Among them, 55 cases of diffuse, LPGC were identified. The histological type of the tumors was determined according to Lauren's criteria and WHO classification. HER2 expression was determined by IHC with monoclonal antibody (Hercept Test) on paraffin-embedded tumor specimen. Overexpression of the HER2 protein was defined as a 3+ positivity with IHC. Gene amplification by FISH was determined when IHC was 2+ positive.

Results: Twenty patients (36.3%) were male and 35 (64%) female. Age ranged from 27 to 85 years, with a median value of 55.7 years. The median follow-up is 1 year. Metastasis was initially present in 39 patients (70.9%). Curative-intent surgery was done in 24 patients (44%) except one who had a partial gastrectomy as a palliative procedure. R0 resection (curative resection with no residual) was achieved in 19 cases and a mean number of 9 lymph nodes were retrieved (range 2-37). 15 patients (27%) received radiotherapy, 11 of them (73%) on adjuvant bases. Therty two (58%) patients received palliative chemotherapy in a metastatic status. The median overall survival for the entire population was 32 months. The survival rates at 12 months were 70% for overall (OS) and 55% for disease free survival (DFS) rates. In a preliminary analysis (20 patients tested), none of the gastric tumors were HER2 positive.

Conclusion: According to the results of our study, LPGC proved to be extremely aggressive histological form, characterized by reduced rate of survival. We confirmed a low rate of HER2 overexpression in this particular group of patients.

Disclosure: All authors have declared no conflicts of interest.

779 USEFULNESS OF STAGING LAPAROSCOPY AND INDUCTION CHEMOTHERAPY WITH S-1 PLUS DOCETAXEL FOR ADVANCED GASTRIC CANCER

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Background: The prognosis of gastric cancer patients with peritoneal metastasis is poor. Therefore, evaluation of the peritoneal metastasis is important to decide the treatment strategy for patients with advanced gastric cancer. Recently, chemotherapy with S-1 based combination therapy has been shown to be highly effective for advanced gastric cancer.

Patients and methods: Between July 2007 and December 2009, staging laparoscopy was performed for 24 patients with advanced gastric cancer at Kumamoto University Hospital. Eleven of 24 patients (46%) had either macroscopic or microscopic peritoneal dissemination and were received induction chemotherapy. The response of peritoneal metastasis to the induction chemotherapy, adverse events and the outcome of the following surgery were retrospectively evaluated.

Results: The median age was 65.4 years (range, 39 –80 years). There were 18 men and 6 women. The number of patients with type2, 3, and 4 tumors were 4, 14, and 6, respectively. The mean tumor size was 9.3cm (range, 3-20cm). Clinical staging before staging laparoscopy were stage II in 5 patients, stage IIIA in 8, stage IIIB in 10, and stage

IV in 1. Eleven of 24 patients (46%) were detected peritoneal metastasis by staging laparoscopy. The number of patients with P1CY1, P1CY0, and P0CY1 were 4, 2, and 5, respectively. These 11 patients underwent induction chemotherapy with S-1 plus Docetaxel. The mean number of courses of S-1 plus Docetaxel was 4.4 (range, 2-10). Four of 11 patients (36%) experienced grade3/4 neutropenia and 3 of 11 (27%) did nonhematological adverse events. When complete response of peritoneal metastasis was defined as disappearance of peritoneal metastasis and negative peritoneal cytology, 4 patients (36%) achieved complete response of peritoneal metastasis. All of these patients underwent R0 resection.

Conclusion: Staging laparoscopy is useful for the diagnosis of peritoneal metastasis in patients with advanced gastric cancer. Peritoneal metastasis of advanced gastric cancer can be successfully treated with S-1 plus Docetaxel. If such patients respond well to the chemotherapy, a curative resection is potentially achieved for them.

Disclosure: All authors have declared no conflicts of interest.

780 TREATMENT FOR PATIENTS WITH CYTOLOGY POSITIVE AND/OR PERITONEAL DISSEMINATION FROM GASTRIC CANCER IN OUR HOSPITAL

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We retrospectively assessed the survival benefit of surgery for patients with cytology positive and/or peritoneal dissemination from gastric cancer.Methods. From 2004 to 2008, 51 patients with cytology positive and/or peritoneal dissemination form gastric cancer visited chemotherapy center after surgery. We evaluate the surgical procedure and prognosis.Result: Gastrectomy was performed 31 (Cure B:4cases,CureC:27cases)of 51 patients. Only staging laparoscopy or gastrojejunostomy was performed 20 of 51 patients. Two of 51 patients couldn't receive first line chemotherapy due to rapid progression after surgery. Forty two patients received oral fluoropirimidine-based chemotherapy(S-1 alone:21cases,S-1+CDDP;12cases,S-1+CPT-11;4cases,Others;5cases)Seven patients received infusional chemotherapy (CPT-11+CDDP :2cases,5FU:5cases).The median survival time was not significantly prolonged in gastrectomy group(623days)compared non-gastrectomy group(495days;p=0.652).Multivariate analysis showed that received S-1+CDDP was the factor that contributed to survival time.Conclusion:The suevival time of patients with cytology positive and/or peritoneal dissemination from gastric cancer was prolonged by the chemotherapy with S-1+CDDP,but no significant prolongation was observed in the patients with gastrectomy.

Disclosure: All authors have declared no conflicts of interest.

781 INFORMATIVITY OF SEROLOGICAL ONCOASSOCIATED MARKER CA 72-4 IN EARLY DIAGNOSTICS OF GASTRIC CANCER RECURRENCE

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Background: to study the value of oncomarker CA 72-4 in early diagnostics of gastric cancer recurrence.

Materials and methods: There examined 70 patients with gastric cancer recurrence. Radical surgery was performed on 15 (21,4%) patients, and 55 (78,6%) unresectable patients received 2-3 cycles of chemotherapy by ELF and FAP regimens. Study was carried out on an empty stomach in dynamic order before and after therapy. Concentration oncomarker in blood up to 6,9 u/ml is considered to be a normal value.

Results: Oncomarker examination after radical surgery in 15patients after 3 weeks showed that in 8 (53,3%) patients oncomarker regression was from 42,4 u/ml up to norm and at the average being 6,4 u/ml , but in 7 (46,7%) patients oncomarker regression was from basic 42,4 u/ml to 10,3 u/ml. Surgery is likely to have conditionally radical character in 7 patients. Oncomarker examination was in normal in 8 patients 2 weeks later after 2nd cycle of chemotherapy, but in 7 patients who were noted some increase of CA 72-4, it was decreased up to norm in 2 patients, no changes were in 3 patients and in 2 patients rise of CA 72-4 level was found. Micrometastases is likely to be eliminated in 2 patients in whom CA 72-4 decreased up norm, but in 5 patients chemotherapy effect was restricted or was not followed at all. 55 (78,6%) patients received chemotherapy. CA 72-4 level was at the average 40,5 u/ml before chemotherapy cycle administration. However, CA 72 -4 in repeated studies were made in 46 (83,6%) patients. According to dynamics of level patients might be divided in 3 groups: First group – 12 patients, in whom CA 72-4 regression was from basic up to 22,2 u/ml and by WHO recommendations partial regression of tumor process was noted. In second group – 16 patients CA 72-4 regression at the average was 31,2 u/ml and it was noted stabilization of the process. In third group – 18 patients, despite they received 2 cycle of chemotherapy, CA 72-4 level was considerably risen and at the average was up to 49,3 u/ml ,here the tendency to progressing was detected.

Conclusions: CA 72-4 study has a large prognostic value not only in early recurrence occurrence but also is an important biological criterion for definition of radical surgery.

Disclosure: All authors have declared no conflicts of interest.

782 EVALUATION OF EPIDEMIOLOGIC FACTORS IN GASTROESOPHAGEAL CANCER IN NORTHEASTERN IRAN

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Aim: To assess the epidemiologic factors related to the incidence of gastroesophageal cancer in northeastern Iran.

Methods: We assessed their ethnicity, sex and age by dividing them into two distinct groups. The first consisted of 395 patients with gastric cancer who had been referred to three oncology centers in Mashhad during the period of march 2003 to September 2008.The second was made up of 144 patients with esophageal cancer had been evaluated from January 2007 to November 2008 in the same oncology centers.

Results: In the first group suffering from gastric cancer, 6.5% were Turk and 93.5% were Fars, 75.9% were male and 24.1% were female. Among these patients the median age for gastric cancer was 63 years for males and 60 years for females. In the second group diagnosed with esophageal cancer, 13.8% were Turk and 86.2% were Fars, 53.5% were male and 46.5% were female. The median age for esophageal cancer was 65 years for males and 62 years for females. Among Turks the incidence of esophageal cancer was higher than that of gastric cancer. In the study the male-female ratio of patients with esophageal cancer was 1.1:1and among patients with gastric cancer this ratio was 3.1:1.

Factors // Gastric cancer total= (395) //Esophageal cancer total= (144).
Race Fars= 93.5% (369) Fars= 86.2 % (124).
Turks= 6.5 % 26 Turks= 13.8% 20.
Sex Male= 75.9 % (300) Male= 53.5% (77).
Female= 24.1% (95)Female= 46.5% (67).
Median Age Male= 63 Years (300) Male= 65 Years (77).
Female = 60 Years (95) Female= 62 Years (67).

Conclusions: In this study Turks of northeastern Iran were more susceptible to esophageal cancer than gastric cancer. In addition the male- female ratio of esophageal cancer was almost equal 1.1:1.These results are significantly different than those reports presented in worldwide.

Disclosure: All authors have declared no conflicts of interest.

783 CLINICOPATHOLOGICAL FEATURES OF DOUBLE PRIMARY CANCERS IN PATIENTS WITH GASTRIC CANCER

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Background: In order to improve the prognosis of gastric cancer patients, the timely identification of second primary cancer is considered to be a crucial clinical problem. And also the pattern of second primary cancers after treatment for gastric cancer is important for patient's survival.

Methods: We analyzed the clinicopathologic data of 5,778 patients with gastric cancer regard to double primary cancers from October 1996 to November 2007. 155 patients with gastric cancer who underwent histopathological confirmation of second primary cancer.

Results: The median age was 61 years, and the male was 95 (61.3%) and female was 60 (38.7%). Associated primary carcinomas were often found in the gastrointestinal tract, especially in the colon (27.1%). The most common histological type of gastric carcinoma was poorly differented adenocarcinoma (43.2%), according Ming and Lauren classification intestinal type (33.5%) and infiltrative type (44.5%) were dominant. 97 metachronous and 58 synchronous second primary cancer had occurred in stomach cancer patients. Median time of Second primary cancer development was 15.8 months, mostly within 10 years of the original surgical treatment. After 10 years, 2 patients of hepatoma and lung cancer were detected. The median survival was 54.2 months. Multivariate analysis showed that gastric cancer stage was related to the survival.

Conclusion: Gastric carcinoma should be treated aggressively and follow up regularly, since the prognosis of gastric cancer related with patient survival. The present study suggests that the follow up of stomach cancer over 10 years is needed in order to enable the early diagnosis of second primary cancers.

Disclosure: All authors have declared no conflicts of interest.

784 THE PREDICTIVE VALUE OF PRE-OPERATIVE BODY COMPOSITION AND HISTOPATHOLOGY ON SURVIVAL POST-PANCREATICODUODENECTOMY IN PANCREATIC CANCER

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Aims: The aim was to assess the pre-operative body composition (BC) status (i.e. weight and components of weight) in patients with resectable ductal pancreatic adenocarcinoma (PCa) presenting for a Whipple's Procedure (WP) and to relate these findings to histopathology and long term survival.

Methods: BC was measured one day pre-operatively in 36 patients (15 M, 21 F), aged 41 to 81 years. Results of Total Body Protein (TBP), Total Body Water (TBW), Fat Mass (FM), and Total Body Potassium (TBK; an indicator of Lean Body Mass) were compared with those of age- and sex-matched controls. Patients' survival and detailed histopathology synoptic reports were documented.

Results: BC: Compared with age- and sex-matched controls, the WP patients had lower TBK (P<0.001). In addition, the body fat was shown to be lower in female (P=0.007) but not in the cohort of male patients. Twelve of 36 (33%) patients had unclear margins and were found to have, compared with the clear margin group, larger tumours and reduced weight (P=0.015), FM (P=0.001), TBP (P=0.045), TBK (P=0.014), TBW (P=0.019) and survival (P=0.036). Histopathology: There were significant correlations between margin involvement and tumour size (P=0.018). Also, vascular invasion was associated with tumour size, (P=0.033), tumour grade (P=0.004) and nodal involvement (P=0.044). Survival: Of the BC parameters tested only FM (P=0.039) predicted survival. Analysis of the pathological parameters indicated that vascular invasion (P=0.001) and margin status (P=0.013) independently predicted survival. There were no significant differences between clear and unclear margin groups in their length of hospital stay.

Conclusions: In comparison with controls, PCa patients had reduced TBK and FM, and the unclear margin subgroup had lower weight and all components of weight. Although, FM was a predictor of survival, the histopathological parameters were stronger predictors of survival. Hence, when a patient presents with significant weight loss, one should be alerted to the association with a more advanced cancer, and surgical treatment should be applied if the radiological characteristics indicate that clear margins can be achieved.

Disclosure: All authors have declared no conflicts of interest.

785 SECOND LINE CHEMOTHERAPY WITH CAPECITABINE (CAP) AND OXALIPLATIN (OX) IN PATIENTS (PT) WITH PANCREATIC OR BILIARY TREE ADENOCARCINOMA (ADC)

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Purpose: Pancreatic and biliary tree ADC represent poor prognostic tumors. Gemcitabine is usually considered the first line chemotherapy and after that no standard treatment has been established. CAP and OX have demonstrated some activity in metastatic (M1) and locally advanced (LA) pancreatic cancer, and the combination of these drugs confers additional benefit as well. We conducted this study in order to establish the efficacy of this schedule on pancreatic and biliary tree ADC.

Patients (pts) and methods: Pts with M1 or LA pancreatic or biliary tree ADC with progression to one previous chemotherapy treatment were included. Performance status<=2, age>=18 years and adequate renal and hepatic function were selected. Schedule of chemotherapy: CAP 1000 mg/m2 bid on days 2 to 15 and OX 130 mg/m2 on day 1 of a 3 week cycle. RECIST criteria were used for assessment of response and NCI-CTCAE v 3.0 for toxicity.

Results: Between April 2006 and March 2010, 40 pt were included. Male/female: 29/11. Mean age: 60.7 years (37-74). Pancreatic/biliary: 23/17. PS 0/1/2: 3/27/10. LA/ M1: 1/39. Mean number of cycles: 2.50 (1-10). Disease response per pt, partial/ stable disease/progression/ not evaluated: 1/9/21/9. Tumor control (partial/stable disease): 10 pt (22%). Hematological toxicity (grade1/2/3/4) (%) per pt: neutropenia 5/2.5/7.5/0; thrombocytopenia 15/5/2.5/5; anemia 42.5/10/52.5/0. Non-hematological toxicity (grade 1/2/3) (%) per pt: asthenia 10/45/17.5; emesis 22.5/15/2.5.; anorexia 12.5/35/7.5; diarrhea 7.5/12.5/5; neurotoxicity 42.5/17.5/2.5; hand-foot syndrome 5/2.5/2.5. One toxic death was reported. Median time to progression: 15 weeks (95% CI 6.6-23.3). Median survival time: 19 weeks (95% CI 10.4-27.5). For pts with PS0 or 1 median overall survival was 23 weeks (95% CI 6.3-39.6) and for pts with PS2 was 8 weeks (95% CI 5.3-1.6) (p 0.004).

Conclusion: Advanced pancreatic and biliar ADC have unfavourable prognosis. After first-line treatment, CAPOX shows a tolerable toxicity and some activity and it can represent an alternative on selected pretreated pts.

Disclosure: All authors have declared no conflicts of interest.

786 FYN-HNRNPA2B1/SAM68 SIGNALING PATHWAY MODULATES BCL-X ALTERNATIVE SPLICING IN PANCREATIC CANCER

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Abstract purpose: Src family kinase Fyn and heterogeneous nuclear ribonucleoprotein(HnRNP)A2B1 have been suggested to associate with the metastasis of tumors, but their roles in regulation of apoptosis is not clear yet. This study is to investigate whether Fyn is via HnRNPA2B1 to regulate apoptosis and metastasis of pancreatic cancer.

Experimental design: We examined the expression of Fyn and HnRNPA2B1 in human pancreatic cancer tissues by immunohistochemistry and systematically investigated the apoptosis mechanisms regulated by the Fyn-A2B1/Sam68 signaling pathway using multiple experimental approaches.

Results: We found that the upregulation of Fyn expression and Fyn activity were associated with the metastasis of pancreatic cancer. In pancreatic cancer BxPc3 cell, inhibition of Fyn activation by kinase dead Fyn(KD-Fyn) not only decreased the cell proliferation and liver metastasis, but also downregulated HnRNPA2B1 expression. Further analysis showed that HnRNPA2B1 expression was associated with pancreatic cancer progression. In BxPc3 cell, the HnRNPA2B1 was bound to Bcl-x mRNA and affected its splicing. Supression of HnRNPA2B1 expression by RNAi increased the formation of proapoptotic Bcl-x(s) and promoted apoptosis of BxPc3 cell. In addition, in BxPc3 cell, activation of Fyn increased the phosphorylation of Sam68 and decreased its binding to Bcl-x mRNA, thereby increases antiapoptotic Bcl-xL formation. Knockdown of Sam68 by RNAi also increased the formation of Bcl-x(L). Finally, expression of HnRNPA2B1 or Sam68RNAi could rescue pancreatic cancer cell from apoptosis induced by KD-Fyn.

Conclusions: Our results suggest a mechanism by which the Fyn-A2B1/Sam68 signaling pathway regulates apoptosis, thus regulating metastasis of pancreatic cancer.

Disclosure: All authors have declared no conflicts of interest.

787 CHEMOTHERAPY SIGNIFICANTLY IMPROVES OVERALL SURVIVAL IN CHOLANGIOCARCINOMA PATIENTS; SINGLE CENTER EXPERIENCE

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Introduction: Surgical resection with R0 margins is the curative treatment in cholangiocarcinoma. In more advanced stages, chemotherapy may increase overall survival with palliative intent. Here in, we report our experience with chemotherapy for such patients in our clinic.

Patients and methods: Charts of 93 patients with advanced cholangiocellular carcinoma not amenable to curatvie therapy followed between periods of 2003 to 2009 at the Baskent University medical Oncology Department were analyzed. . Mean age of patients was 63 years (range 34-87). Forty one (44.1%) and 52 (55.9%) patients were male and female, respectively.

Results: Common risk factors like hepatitis B infection, hepatitis C infection, diabetes mellitus, obesity, and cholelithiasis defined in 1(1.5%), 5 (7.6%), 16 (26.2%), 8 (16%), and 28 (35.9%) patients respectively. Palliative biliary drainage was the first treatment modality in 53 (63.9%) patients. Median overall survival (OS) was 6.1 months (95% confidence interval [95%CI], 3.1-9.2) in whole population. Cytotoxic chemotherapy was administered to 41 patients (44.1%). In patients receiving chemotherapy, the OS was 12.9 months, whereas in those who were only on best supportive care, it was only 2.1 months (p=0.002). Survival analyses failed to show significant difference between patients treated with cisplatin or fluorouracil based chemotherapy in terms of both OS and progression free survival. However, ECOG performance scale in chemotherapy group was significantly better than other group (Fischer's exact test, p =0.045). When the patients with ECOG performance with 3 and 4 were excluded, OS in chemotherapy group was still better (2.1 months) than non-chemotherapy group (12.9 months), significantly (p=0.004). Only ECOG performance status and systemic chemotherapy showed statistically significant effect on OS in univariate analyses.

Discussion: Metastatic cholangiocarcinoma is incurable disease with poor prognosis and relatively short survival. Systemic chemotherapy significantly improves overall survival in patients who have good performance score.

Disclosure: All authors have declared no conflicts of interest.

788 PHASE II STUDY OF FIXED DOSE-RATE INFUSION OF GEMCITABINE AND UFT COMBINATION CHEMOTHERAPY IN PATIENTS WITH ADVANCED BILE DUCT CANCER: DAEGU GYEOUNGBUK ONCOLOGY GROUP

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Purpose: This phase II study evaluated efficacy of fixed dose rate (FDR) infusion of gemcitabine (10mg/m^2/min) and UFT combination in chemo-naïve patients with advanced bile duct cancer.

Patients and methods: This was an open-label, single-arm, multicenter, phase II study with a Simon two-stage minimax design. Patients received the FDR gemcitabine 1000mg/m^2 for 3 consecutive weeks and UFT 400mg/m^2 on days 1-21. The cycle was repeated every 28 days. The primary end point was Response Evaluation Criteria in Solid Tumors (RECIST) -defined objective response rate. Secondary end points included clinical benefit response (CBR), safety, progression-free survival (PFS), and overall survival (OS). Clinical characteristics including four single nucleotide polymorphisms in DNA repair genes (RecQ1, RAD54L, XRCC1, ATM) were evaluated whether these influence the overall survival.

Results: Between December 2006 and February 2008, fifty-one patients were enrolled, with a median age of 58 years. The majority of patients (76%) had intra-hepatic disease. Fourteen patients (27%) had a RECIST investigator-assessed, partial response (PR); disease control rate (PR + stable disease) was 55%. CBR was 14% among 37 evaluable patients. Hematologic toxicity was main grade 3 or 4 treatment-related adverse events. Median PFS was 4.0 months (95% CI, 2.9 to 5.1 months). Median OS was 7.0 months (95% CI, 3.5 to 10.5 months). Intrahepatic disease, poor performance, and, XRCC1 R194W C/C type were predictive markers of poor overall survival.

Conclusion: FDR gemcitabine and UFT demonstrated apparent activity in patients with advanced bile duct cancer. However, this activity did not translate to prolong survival. The location of disease, performance status, and, polymorphic variants of DNA repair genes may affect clinical outcome of patients with advanced bile duct cancer.

Disclosure: All authors have declared no conflicts of interest.

789 SURGICAL RESECTION AFTER DOWN-STAGING CHEMOTHERAPY FOR INITIALLY UNRESECTABLE BILIARY TRACT CANCER

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Background: Surgical resection is currently the only curative treatment strategy for biliary tract cancer. However, It has been estimated that a curative resection can only be performed in 40-70% of all patients presenting with biliary tract cancer. Recently, an improved efficacy has resulted in the possibility for patients with initially unresectable biliary tract cancer to undergo curative surgical resection after downsizing of cancer by chemotherapy. The aim of this study was to evaluate the effect of systemic chemotherapy in patients with initially unresectable birliary tract cancer.

Patients and methods: Since 2006, 18 patients with radiographically unresectable, locally advanced biliary tract cancer have received gemcitabine alone or gemcitabine-based systemic chemotherapy. The underlying biliary diseases in these patients were intrahepatic cholangiocarcinoma in 5 patients, extrahepatic chalangiocarcinoma in 8 patients, and gallbladder carcinoma in 5 patients. The reasons for the definition of unresectability were extensive vascular infiltration in 13 patients (eight arterial infiltrations, three portal vein infiltrations, three venous infiltrations) and extensive liver involvement in 5 patients. Response to chemotherapy was evaluated every 2 months using enhanced CT scan. Patients responding to chemotherapy were reconsidered whether the tumor was resectable.

Results: Four of 18 (22%) patients had an objective response and underwent curative surgical resection with extensive hepatic resection and bile duct resection after chemotherapy. Concomitant vascular resection was required in three patients (inferior vena cava resection and reconstruction in 2, portal vein resection and reconstruction in 1). With a median follow-up of 17 months, median survival for the resected patients was 35 months. Median survival was 10 months in the nonresponder group. Three specimens presented a major pathological response at hitological examination.

Conclusion: Initially unresectable biliary tract cancer may be downstaged by gemcitabine- based chemotherapy to allow for surgical resection. This approach increased median survival and may have a potential for disease eradication as a new strategy for the initially unresectable patients with locally advanced biliary tract cancer.

Disclosure: All authors have declared no conflicts of interest.

790 HEPATIC RESECTION FOR HEPATOCELLULAR CARCINOMA

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Background: The question of treatment strategy of a hepatocellular cancer (HCC), depending on prevalence of tumor and preserved liver function, is widely discussed now.

Material and methods: Between 1990 and 2009, 171 patients with HCC underwent liver resection. Fifty eight patients had virus hepatitis, among this 54% - hepatitis B, 34% - hepatitis C, hepatitis TTV and G at 8% and 4%. Fifty five patients had cirrhosis (Child A - 64%, Child B - 36%). In according to Barcelona Clinic Liver Cancer Staging Classification (BCLC), the early stage (A) is diagnosed for 59%, intermediate stage (B) at 20%, and advanced stage (C) at 21%. The major liver resections were carried out in 71% of cases and 22 patients, among them, had cirrhosis (Child A - 14, Child B - 8).

Results: Postoperative morbidity is diagnosed in 44.6 % of cases and mortality is in 5.7%. There were insignificant difference in morbidity (50.2% against 47.4%) and mortality (6% against 5%) after major and sparing resections. The cirrhosis background has negative short-term results. Postoperative morbidity without cirrhosis and on cirrhosis stage Child A, Child B are diagnosed as 41%, 39.3%, 75%, and as 2.1%, 7.1%, 25% of mortality. The 5, 10 and 20-year overall survival rates were 53.5%, 37.3% and 28.8%. The 5-year survival rate on A,B,C, stages (BCLC) were 69.1%, 30.9%, 26.4% and the 10-year were 51.6%, 10.3% and 0%.

Conclusion: Surgical resection is expedient in patients with HCC. Radical resection if feasible is suggested in patients with HCC, B and C stages (BCLC), because it prolongs survival. We don't recommend the liver resection in patients with HCC and cirrhosis stage Child B by reason of bad short-term results.

Disclosure: All authors have declared no conflicts of interest.

791 A PHASE I/II TRIAL OF CONTINUOUS HEPATIC INTRA-ARTERIAL INFUSION OF 5-FLUOROURACIL, MITOXANTRONE AND CISPLATIN (FMP THERAPY) FOR ADVANCED HEPATOCELLULAR CARCINOMA

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Background: The aim of this study was to investigate the maximum-tolerated dose and determine the recommended dose, based on the frequency of dose-limiting toxicities, of continuous hepatic intra-arterial infusion of 5-fluorouracil, mitoxantrone and cisplatin (FMP therapy) in a phase I study protocol, and to evaluate the efficacy and toxicity of FMP therapy at the recommended dose for advanced hepatocellular carcinoma (HCC) in a phase II study protocol.

Methods: Forty-five patients with advanced HCC who were not candidates for surgical resection, local ablation or transcatheter arterial embolization, had no history of prior chemotherapy, were enrolled. The therapy consisted of intra-arterial administration of cisplatin (P) and mitoxantrone (M) on day 1, and continuous intra-arterial infusion of 5-fluorouracil (F) from day 1 through day 5 [F/M/P(mg/m2): Level1; 400/4/60, Level 2; 400/6/60, Level 3; 500/6/60]. The treatment was repeated every four weeks for a maximum of six courses, until the appearance of evidence of tumor progression or of unacceptable toxicity.

Results: In the phase I part of the study, one of six patients at level 1 developed DLT, including grade 3 pulmonary embolism, while none of the patients at either level 2 or 3 exhibited any signs of dose-limiting toxicity. Therefore, the recommended dose of FMP therapy was determined to be the level 3 dose. In the phase II part, 36 patients were enrolled. Nine patients (25%) achieved a partial response, and the response rate was 25% (95% confidence interval: 12-42%). The overall median survival time, 1-year survival rate and median progression-free survival were 11.3 months, 46.9% and 7.0 months, respectively. The main grade 3 and 4 hematological and non-hematological toxicities were leukopenia (36%), neutropenia (39%) and thrombocytopenia (19%), and elevation of the serum levels of aspartate aminotransferase (22%) and alanine aminotransferase (14%). These toxicities were generally transient and well-tolerated.

Conclusion: In patients with advanced HCC, hepatic arterial infusion of FMP was feasible, however, no favorable tumor response or survival benefit could be demonstrated.

Disclosure: All authors have declared no conflicts of interest.

792 DEEP ELECTRO-HYPERTHERMIA WITH OR WITHOUT THERMO-ACTIVE DRUGS : OUR EXPERIENCE IN PATIENTS WITH ADVANCED HEPATIC CELL CARCINOMA (HCC)

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Until 2008 advanced HCC has no standard chemotherapy. We evaluated effectiveness and toxicity of capacitatively coupled low-frequency 13.56 MHz deep hyperthermia (EHY 2000) treatment on HCC which underwent all other possible treatment.

Methods: From 02/2005 to 09/2009, we enrolled 63 pts with advanced HCC. Median age was 69 y (range 61 -78), pts male/female were 53/10. 47,6% of pts were un-eligible for liver surgery or other loco-regional therapy , 33% of pts underwent sequential multi therapy treatment . 17,5% of pts were pre-treated with surgery, 9,5% TACE, 4,8% PEI or TARF. All pts were in stage C of BCLC classification. 33,3% of pts had metastasis (11% bone retroperitoneal, peritoneal, soft tissue, lung, 20,6 % node , 38,1% portal vein thromboses) . 19 pts underwent only to EHY owing to clinical conditions . Schedule : EHY was achieved by arrangements of capacitative electrodes with a radiofrequency field of 13.56 Mhz (RF-DHT) at 80- 130 W equivalent to 41 °- 47° C for 60 minutes, 2 times/w for 5 weeks plus thermo-active agents (TAA). EHY was applied over 2 time a week over 1 hour as mono - combined therapy . TAA was oxaliplatin 50 mgr at fixed dose on D 1 and D 15 in 16% of pts or cisplatin 20 – 25 mg at fixed dose/w for 5 administrations in 54% of pts. 10 applications of EHY are 1 cycle, Median number of cycles was 1,5 (range 1-4), total EHY applications were more then 650.

Results: EHY plus TAA had had clinical benefict with an excellent compliance on out-patients. We observed 1 CR, PR, 3,6% , 36,5% of SD. Median survival time was 7,5 + (range 1 – 62) mths for al pts and 9,6 mths in pts with portal thrombosis. 16 pts presented evidence of increasing well-being: someone stopped or reduced analgesic therapy or they referred a reduction of anxiety. OS after 6 mths is 46% (29 pts), at 1 year 13,1 % (8 pts). Toxicity: only 6 pts had skin reaction . 3 pts treated with medium electrode debelopped cutaneous hyperemia on the area of treatment and mild burn on the Skin; all symptoms disappeared after local steroid therapy , EHY was stopped until resolution.

Conclusions: Clinical benefit and Low toxicity will be confirmed in further clinical studies. Capacitively coupled low-frequency 13.56 EHY is feasible for chemorefractory HCC.

Disclosure: All authors have declared no conflicts of interest.

793 INITIAL TREATMENT DOSE AND REASONS FOR DOSE ADJUSTMENT DURING ORAL CAPECITABINE CHEMOTHERAPY

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Objective: The aim of this study was to observe doctors' adherence to therapeutic standard and dose modifications during therapy in a prospective observational study of capecitabine in GI cancer. In colorectal cancer patients, standard doses were 1000 and 1250 mg/m^2 bid for monotherapy and combination therapy, respectively, and 825 mg/m^2 bid with radiotherapy. For pancreatic and gastric cancer patients, doses were 650 and 825 mg/m^2 bid, respectively.

Methods: All data were collected prospectively. Medication dose and adjustments (including reasons) were collected at each of 6 consecutive visits and adverse events documented.

Results: In this final analysis, 52 physicians provided data on 243 patients (40% male) receiving capecitabine-based therapy, of which 55% had colorectal, 23% breast, 10% gastric and 9% pancreatic cancer. Of these, 43% received combination therapy (+/- biologic), 47% monotherapy (+/- biologic) and 10% chemoradiation. The starting dose of capecitabine was lower than standard in 38% of patients, at standard dose in 41% of patients, and above standard in 21% of patients. 29% had no dose adjustments, 36% dropped out due to PD/lack of efficacy, while 35% had dose adjustments during therapy mainly because of adverse events (49%), patient request (18%), no response to treatment (13%), reduced weight (7%), co-morbidity (4%) or other (16%). While the overall starting dose was independent of age, elderly patients (>65 years) had slightly more dose adjustments. Independent of indication, patients starting above standard dose did decrease dose with time but remained above standard at the end of treatment, while patients starting at standard dose or below maintained this level throughout treatment, while the rate of adverse events was similar.

Conclusions: The majority (62%) of patients received capecitabine at the labeled dose or above. About half of these had dose adjustment during treatment because of toxicity or at their request. It has previously been shown to be possible to adjust capecitabine dose to manage side effects without compromising efficacy. Here we show that patients initiated at the standard dose usually do not need dose adjustments during the course of treatment, regardless of indication.

Disclosure: R. von Moos: Compensated consultant / advisory board member for F. Hoffmann-La Roche, Amgen, Novartis Speaker honoraria from F. Hoffmann-La Roche, Amgen. M. van Lier: Employee; product manager, F. Hoffmann-La Roche. S. Nick: Employee; medical manager, F. Hoffmann-La Roche. R. Winterhalder: Consultant / advisory board member for F. Hoffmann-La Roche. All other authors have declared no conflicts of interest.

794 IMPACT OF DIFFERENT PATIENT MANAGEMENT APPROACHES ON THE CONTROL OF CAPECITABINE-RELATED ADVERSE EVENTS: A PROSPECTIVE COHORT ANALYSIS FROM SAEDA II

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Background: A previous cohort analysis showed high compliance with capecitabine independent of age or ECOG status [SAEDA I; Winterhalder et al. ASCO GI 2009]. This prospective cohort analysis of patients receiving capecitabine-based chemotherapy aimed to identify patient management approaches to improve adverse-event (AE) control, which may further increase compliance and therapeutic outcome.

Results: Between December 2008 and January 2010 a total of 52 oncologists recruited 157 patients with GI cancer. Median age was 67 years (range 40–90) and 40% of patients were male. 74% had colorectal, 13% pancreatic and 13% gastric cancer. Compliance was high (90%) and was independent of age and ECOG status. Most frequent AEs were nausea/vomiting, hand-foot-syndrome (HFS), diarrhea and loss of appetite. Non-compliant patients had a higher rate of nausea (54% vs. 43%), vomiting (16% vs. 14%) and depression (15% vs. 3%) than compliant patients. Elderly patients (<65 vs 70 yrs) had more side effects than the younger patients (<65, 1.74 vs 1.49; <70, 1.66 vs 1.51), mainly due to higher rates of nausea/vomiting. Of the patient support provided patients receiving >20 min of patient education dialogue had less AEs than those with <20 min (1.49 vs 1.84). In addition, patients using patient diaries had a better rate of AE-control (1.40 vs 1.68). No impact was observed from patient brochures, tablet box or a patient AE-information card.

Conclusions: This final analysis indicates that patients are highly compliant with capecitabine, irrespective of age and ECOG status. Compliance is negatively influenced by nausea, vomiting and loss of appetite, which interact directly with the oral application of the medication. Doctors actively providing patient support are more successful in the control of AEs. The total time spent on patient education and patient diaries can improve AE control.

Disclosure: R. Winterhalder: Consultant / advisory board member for F. Hoffmann-La Roche. M. van Lier: Employee, product manager, F. Hoffmann-La Roche. S. Nick: Employee, medical manager, F. Hoffmann-La Roche. R. von Moos: Compensated consultant / advisory board member for F. Hoffmann-La Roche, Amgen, Novartis Speaker honoraria from F. Hoffmann-La Roche, Amgen. All other authors have declared no conflicts of interest.

795 SURGICAL APPROACH TO NON-COLORECTAL LIVER METASTASES : EGE UNIVERSITY EXPERIENCE

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Aim: In this study we aimed to retrospectively analyze the patients who were admitted to Ege University Faculty of Medicine (departments of general surgery and medical oncology) with non colorectal metastases between 2003-2008, by means of demographic properties, operability conditions and site of primary tumor.

Material and methods: A total number of 78 patients with non-colorectal liver metastases were included. File recordings, operation notes and pathological

examinations of these patients were retrospectively analyzed. All the recorded data were analyzed with SPSS 12.0.

Results: Forty three (55%) of the 78 analyzed patients were male. The mean age was 56.3. The majority of the primary tumors were localized in the abdominal viscera (72% n=56). The most encountered primary tumor site among these was pancreas (28% n=22). Other primary tumor sites according to their frequency follows as stomach (24% n=19), gal bladder (%12 n=9) and small intestine (7,6% n=6). The remainder primary tumor sites show a wide range of distribution, including breast carcinoma, synovial sarcoma and malignant melanoma. The most common histological type was adenocancer (67%, n=52). Most of the patients received diagnostic surgical procedures; definitive procedures such as liver resections were possible only in 26 patients (34%). More than half of the patients who underwent liver resection had gastric cancer.

Discussion: Liver resection should be kept as an option in case of long disease free survival and solitary metastases in non colorectal liver metastases.

Disclosure: All authors have declared no conflicts of interest.

796 TSER AND MTHFR GENE POLYMORPHISMS AND TOXICITY IN CANCER PATIENTS TREATED WITH FLUOROPYRIMIDINE BASED CHEMOTHERAPY

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Aim of the study: to investigate the association of the thymidylate synthase (TS) and methylenetetrahydrofolate reductase (MTHFR) gene polymorphisms with the grade of toxicity in cancer patients treated with fluoropyrimidine based adjuvant chemotherapy.

Patients and methods: We evaluated 36 consecutively observed patients: 17 pts radically resected for gastric cancer and treated with radiotherapy and fluoropyrimidine (5/FU C.I.:10 pts; capecitabine: 7 pts) and 19 pts for radically resected for colon cancer treated with fluoropyrimidine alone (5/FU C.I.: 2 pts; capecitabine: 17 pts). Hematological and not hematological toxicity was graded according to WHO criteria. The TS (28 bp TSER) and MTHFR (A12989T, C677T) polymorphism were detected in blood samples using pyrosequencing system. Statistical analysis included the T Test; a p value < 0,05 was considered statistically significant.

Results: Patients with the TSER 3R/3R genotype had a lower incidence of grade 2/3 toxicity than patients with 2R/2R and 2R/3R genotypes (p = 0.05) (Table). Patients with the MTHFR 677 C/C genotype had a lower G2-G3 toxicity incidence (p <0.05). No significant association was found between MTHFR A1298C polymorphisms and chemotherapy toxicity.

Conclusions: The TSER and MTHFR C677T polymorphisms showed an association with fluoropyrimidine toxicity in the adjuvant setting of colon and gastric cancer patients.

	Toxicity	
Genotype	G0/G1 n (%)	G2/G3 n (%)
TSER - 2R/2R - 2R/3R - 3R/3R	6 (67) 8 (72) 13 (87)	3 (23) 3 (28) 2 (13) p=0,05
MTHFR A1298C - A/A - A/C - C/C	9 (70) 14 (82) 4 (67)	4 (30) 3 (18) 2 (23) p=0,111
MTHFR C677T - C/C - C/T - T/T	13 (87) 10 (77) 5 (63)	3 (13) 2 (23) 3 (27) p <0,05

Disclosure: All authors have declared no conflicts of interest.

797 TRENDS IN GASTROINTESTINAL CANCER REFERRALS IN ACUTE HOSPITALS IN LONDON, UK

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Introduction: Upper gastrointestinal (UGI) and lower gastrointestinal (LGI) cancers accounted for 8% and 12.5% of 10 commonest cancers occurring in the UK and Ireland during the 1990s. Although there is little geographical variation in incidence and mortality for all cancers combined, there appears to be some variation for certain types of cancer.

Aims and methods: To analyze trends in the number of suspected UGI and LGI cancer referrals for all London Acute NHS Hospital Trusts (AHT) between 2007-2008.

Data for suspected UGI and LGI cancer referrals seen during the quarter for each AHT in the London area was compared.

Names of London AHTs were obtained from the NHS website. AHTs were into their previous respective Strategic Health Authority (SHAs)localities. Resident population estimates (2004 mid-year estimates) for the 5 former London SHAs were based on the ONS National Population Census 2001. Summary statistics were calculated

Results: There were 109,536 UGI and 182,479 LGI suspected cancer referrals for England over 2007-2008, of which 8,900 UGI and 18,757 LGI suspected cancer referrals were from London. Significant variation was seen in the numbers of suspected UGI and LGI Cancer Referrals in each SHA (ratio between lowest (North West London) and highest (North East London) being 3.3.London has significantly lower rates of Suspected UGI (0.12%) and LGI Cancer Referrals (0.25%) than England (UGI 0.22%, LGI 0.37%)(p=0.00001). Population adjusted referral rates ranked Noth Est London, South East London, South West London, North Central London, and North West London highest to lowest for suspected UGI cancer referrals and South East London, North East London, South West London, North West London, and North Central London highest to lowest for suspected LGI cancer referrals. London suspected UGI/LGI cancer referrals accounted for 8%/10% of all England referrals respectively. Moreover essentially equal levels of deprivation existed in all 5 former SHAs.

Conclusion: In summary, although marked variation exists in the number of suspected UGI and lower GI cancer referrals amongst the 5 former SHAs in London, the overall rates of suspected cancer referrals in London are significantly lower than for the rest of England.

Disclosure: All authors have declared no conflicts of interest.

798 PHASE II STUDY OF GEMCITABINE AND OXALIPLATIN IN UNRESECTABLE GALL BLADDER CANCER

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Purpose: Oxaliplatin and Gemcitabine are active in the treatment of Advanced Gastrointestinal tract malignancy. We conduct a phase II study to evaluate efficacy and safety of Oxaliplatin and gemcitabibe combination in unresectable Gall Bladder Cancer. Design Drugs gemcitabine 1000 mg/m2 on day 1 and oxaliplatin 85 mg/m2 IV infusion on day 2; 3 weeks cycle for a maximum of six cycles or unacceptable toxicity which ever was earlier.

Materials and methods: Thirty five patients were enrolled and analysis was restricted to 34 who were treated. Median age was 42 years and 21 patients were females.

Results: CR 4 (11.76%), PR 7 (20.58%), SD 10 (29.41%), and PD 12. One had complete pathological response. Median OS and PFS were 8.5 and 4 months, respectively. OS in responders was 11.2 versus 5 months in non-responders (p < 0.0000). Twelve patients (35%) survived for a year or more. There was no toxic death and grade III/IV toxicity seen in 10 (29%) patients: diarrhea 3, vomiting 2, neutropenia and thrombocytopenia 5 patients.

Conclusion: This combination of Oxaliplatin and Gemcitabine is effective in unresectable GBC. It need further evaluation in large population to be considered as a new treatment option of unresectable gall bladder cancer.

Disclosure: All authors have declared no conflicts of interest.

799 A RETROSPECTIVE ANALYSIS OF GALLBLADDER CANCER PATIENTS REFERRED TO THE NATIONAL CANCER INSTITUTE IN MEXICO BETWEEN 2004-2009

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Introduction: Gallbladder cancer is the most common malignant tumor of the biliary tract. It is associated with a desolate prognosis, with a 5-year survival rate of 5%. There are some parts of the world where the incidence is comparatively high, contributing to a health problem as a result of its associated poor outcome. All the statistics mentioned above comes from developed countries. We decided to do this research to know what is happening in our country, specifically in our hospital.

Methods: A retrospective analysis of gallbladder cancer patients referred to the National Cancer Institute in Mexico from 2004 to 2009 was performed. For the analysis we have used SPSS version 17.

Results: 46 patients were identified. The mean age was 61.5 years (range 35-80). Most of the patients were female (71.7%). 89.1% were adenocarcinoma meanwhile 10.9% were squamous. According to TNM there were 8.6% stage I, 41.3% stage II, 2.2 % and 43.5% stage III and IV respectively. Two cases were not classified. Mean time from

the beginning of the symptoms and the first giving treatment was 220 days (range 102-338). We examined different prognostic factors for overall survival finding that only albumin levels were significant (95% IC 0.098-.765; p=0.013) **Figure 1.** Serum alkaline phosphatase was significantly elevated in 63% of patients (from 127 until 1182 UI/L). Gallbladder cancer was incidentally found in thirty three patients during cholecystectomy (71.7 %), none of these were re-explored. 39% of the patients were treated with palliative chemotherapy, 21% to palliative radiotherapy meanwhile 24% with the best support care. In our Institution, the initial treatment was performed only in 21% of all cases (n=15), notice that 60% were stage IV. From this subgroup, 60% received a palliative treatment with chemo or radiotherapy, and 40% with just the best support care.

Conclusion: A high percentage of our patients have been initially treated by a non oncologist surgeon, and/or come to our institution with an advanced disease. We found out that most of them presented decreased serum albumin levels (<3.5 g/dl) and we suggest that this is an adverse prognostic factor for overall survival.

Figure 1. Survival Distribution Function

Months	Albumin <3.5g/dl	Albumin ≥ 3.5g/dl
0	100%	100%
5	71%	91%
10	40%	78%
20	12%	58%

Disclosure: All authors have declared no conflicts of interest.