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Introduction. Bisphosphonates are comprehensively established in the treatment of metastatic bone disease and significantly reduce skeletal morbidity. Zoledronic acid (Zometa®) has a well established role as first-line treatment in patients with bone metastases secondary to breast cancer. Moreover preclinical studies have demonstrated that it can inhibit angiogenesis, invasion and adhesion of tumor cells.

Materials and methods. We retrospectively analyzed 326 metastatic breast cancer patients treated between January 2003 and October 2009 at the Department of Radiation-Oncology of the University of Florence.

We administered a total of 3345 cycles of intravenous zoledronic acid (15 minutes infusion) with a mean of 10 courses (range 6-39). Clinical efficacy assessments and evaluation of new skeletal-related events were performed at each visit. Measures of bone-pain scores and analgesic consumption were evaluated using a patient-rated scoring system. Similarly, analgesic use was scored on a 7-point scale. The effect of zoledronic acid on bone pain and analgesic use were evaluated by averaging the bone pain score and the analgesic use score and assessing their variation from baseline during the whole treatment. Laboratory tests were performed at baseline and at each visit while efficacy assessments were performed when planned or if necessary. Concomitant medications and adverse events were documented according to WHO criteria.

Results. At a median follow-up of 23.5 months (range 6-58) the mean pain score decreased from 2.1 at baseline to 1.80 and the mean analgesic score from 1.65 at baseline to 1.35 during the whole follow-up period. Zoledronic acid was generally well tolerated; we had no grade 3-4 adverse events. No patient had severe deterioration of renal function. Three patients (1%) developed bisphosphonate-associated osteonecrosis of the jaw.

Conclusions. In our experience zoledronic acid confirmed its main role in quality of life among metastatic breast cancer patients, with an optimal toxicity profile. New trials are required to show its potential to delay cancer treatment-induced bone loss in patients receiving hormonal therapies and its antitumor properties.

G19 NEW COMBINATION OF LYPOSOMAL ANTHRACYLINE, CISPLATIN AND METRONOMIC CAPECITABINE AS PREOPERATIVE CHEMOTHERAPY FOR OPERABLE AND LOCALLY ADVANCED BREAST CANCER: DATA OF EFFICACY AND TOLERABILITY

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Background. The main goal of preoperative chemotherapy is the achievement of pathological complete remission (pCR). We report the data of activity and safety of the anthracycline-containing regimen MCX with the introduction of oral fluoropyrimidine capecitabine as preoperative chemotherapy for large operable and locally advanced breast cancer.

Methods. Patients with operable breast cancer (T2-T3) or locally advanced breast cancer (T4, N2-N3) were treated with non-pegylated liposomal doxorubicin (Myocet 50 mg/m^2 day 1), cisplatin 60 mg/m^2 day 1 and metronomic capecitabine 1500 mg daily continuously (MCX) for six courses followed by radical surgery and radiotherapy**.** In patients whose tumours were endocrine-responsive concurrent endocrine therapies (letrozole if postmenopausal or triptorelin if premenopausal) were given preoperatively. All patients had a core biopsy and a basal surgical evaluation to define type of surgery.

Results. Twenty patients were enrolled. Median age was 51 years (range 29-71), premenopausal 44%. At the core biopsy: ER and/or PgR >1% in 60%, Ki-67 expression ≥20% in 67%, HER-2/neu negative in all patients. Clinical stage at diagnosis was: II B in 20%, IIIA in 30%, IIIB in 35%, IIIC in 15%. Sixteen patients are evaluable for clinical response, thirteen patients are evaluable also for pathological response. There were 4 pCR (4/13, 30%), 12 partial remissions (PR) (9/16, 75%) and 4 complete remissions (CR) (4/16, 25%). Six patients out of 13 received breast conserving surgery. The worst toxicity was non febrile grade 4 neutropenia in 2 pts (15%), grade 3 anemia in 1 pt (8%), nausea/emesis grade 2 in 10 pts (50%) and alopecia in 6 (37%). No cardiac toxicity was observed.

Conclusions. This combination is effective as preoperative treatment. The possibility to combine oral fluoropyrimidine capecitabine as metronomic delivery in an anthracycline-containing regimen is promising in terms of clinical activity and safety.

G20 WEEKLY DOCETAXEL (wDOC) FOR THE TREATMENT OF METASTATIC BREAST CANCER (MBC): A LITERATURE BASED META-ANALYSIS (MA)

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MBC accounts for <10% of newly diagnosed BC patients and about 30% of early BC patients will recur. The taxanes represent a milestone in the treatment of MBC. In 2005, Ghersi published a MA comparing taxanes versus non-taxanes containing regimens for MBC finding docetaxel combinations significantly improving OS. To reduce the >80% G3-4 neutropenia and non-hematologic toxicities associated with the docetaxel 3-weekly schedule (3wDOC), weekly schedules have been tested in several phase I/II studies. Unfortunately most of the phase III trials have been prematurely closed due to small samples recruited.

To evaluate the activity (ORR) and tolerability (G3-4 neutropenia) of wDOC, alone or in combination, compared to the 3wDOC schedule, we performed a meta-analysis of all the published papers and abstracts exploring this issue. An electronic (MEDLINE, Cochrane) and manual (ASCO, ESMO, SABCS proceedings, references of selected articles, published reviews) thorough search has been performed. From the available data we collected the necessary informations (ORR, G3-4 neutropenia, median OS and TTP).

We included 8/378 studies (9 comparisons, 742 pts, 368

wDOC, 374 3wDOC). No significant difference in terms of ORR was observed between wDOC and 3wDOC (odds ratio -OR-1.46, 99% CI 0.97-2.19; p >0.01). Interestingly, a highly significant difference was observed in terms of G3-4 neutropenia incidence (OR 0.16, 99% CI 0.05-0.46; p <0.01). The risk difference (RD) for ORR and G3-4 neutropenia has been evaluated showing wDOC is significantly risk-reducing for severe neutropenia (RD -0.3, 99% CI -0.52 – -0.07, p <0.01).

In conclusion our MA supports the administration of wDOC for the treatment of MBC particularly in pre-treated, elderly or poor PS patients for which a combination with other active chemotherapeutic agents is planned. Final survival data emerging from our MA will be shown.

G21 HEREDITARY AND FAMILIAL BREAST CANCER IN SOUTHERN ITALY: RESULTS OF A SURVEILLANCE PROGRAM TARGETED ON RISK PROFILE

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Introduction. BRCA1/2 carriers and women at hereditary/familial risk for breast cancer (BC) may undergo intensive surveillance.

Aim. We report the results of our surveillance program proposed as operative model within oncogenetic counselling for the management of subjects at risk.

Methods. The surveillance program was designed on specific risk profile (hereditary and familial) according with Modena criteria and mutation status. BC, other sites cancers and premalignant lesions have been analyzed according to risk profile, age groups, healthy condition (unaffected/affected) and years of follow-up. Statistical analysis was performed applying Chi-square test.

Results. A total of 325 subjects (193 unaffected; 132 previous cancer) underwent our surveillance program. Age at surveillance program entry: ≤40 yrs (40.7%), 41-50 yrs (25.3%) and >50yrs (34.0%). Subjects were distributed in two risk categories: 241 hereditary and 83 familial clustering. Genetic testing was performed in 76 subjects showing 25 BRCA mutation carriers (12 BRCA1; 13 BRCA2).

At a median follow-up of 1.16 years (range 0-12.62), 25 tumours were detected, of which 18 (68%) in affected subjects and 7 (32%) in unaffected subjects. A significant risk of second malignancies was found for subjects with a previous cancer (OR = 3.3, 95% CI 1.03-8.3) compared with unaffected subjects (p = 0.01). Tumours occurred in different sites: 16 breast (4 omolateral, 4 contralateral and 8 new cancer) and 9 other body sites (2 ovary, 1 endometrium, 1 colon, 2 melanoma *in situ*, 1 basalioma, 1 mediastinum, 1 leukemia). Tumours were more frequently diagnosed in hereditary group (68%) compared with familial group (32%) (p = 0.715). Moreover, 17 premalignant lesions were diagnosed (10 breast, 3 skin, 2 colon, 1 endometrium, 1 bladder). No statistically significant differences were reported in diagnosis of premalignant lesions between affected and unaffected groups.

Conclusion. Our surveillance program targeted on risk profile suggests the need to identify subjects at hereditary/familial risk, generally excluded from screening program.

G22 CORRELATION BETWEEN BREAST CANCER DIFFUSION-WEIGHTED IMAGING (DWI) AND HISTOPATHOLOGICAL CHARACTERISTICS

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Purpose. Diffusion weighted imaging (DWI) is a magnetic resonance imaging (MRI) technique that measures the exchange of water molecules between tissue compartments. Compared with benign breast nodules, malignant lesions are characterized by small restrictions in the free movement of water, which can be quantified by the Apparent Diffusion Coefficient (ADC). We sought to study whether ADC values could also correlate with histopathological breast cancer features.

Patients and methods. We analyzed 160 breast cancers in 158 patients undergoing DWI-MRI before surgery. For each breast cancer, the ADC value was obtained analyzing a region of interest (ROI) traced within the lesion by the Functool software (GE Healthcare). The relationship between ADC and tumor diameter, Ki-67, and estrogen-receptor (ER) expression was studied by linear regression analysis. Mean ADC values according to tumor histology (ductal vs others), tumor grade (1-2 vs 3), hormone-receptor status, and HER-2 status were compared by Student's *t*-test. Additionally, mean ADC values were compared by analysis of variance (ANOVA) in groups defined by the following immunohistochemical surrogates of the intrinsic subtypes: Luminal A (ER+/HER-2-negative/$Ki67_{low}$), Luminal B (ER+ and either HER-2-positive or $Ki67_{high}$), HER-2-enriched (ER-/HER-2-positive) and basal-like (ER-/HER-2-negative).

Results. The mean ADC value was 1.036 (0.470-2.420). No significant relationship was observed between ADC values and tumor diameter, Ki67 values and ER levels. Furthermore, mean ADC values did not differ according to tumor histology, grade, hormone receptor status and HER-2 status. However, when analyzing immunohistochemically defined intrinsic subtypes, Luminal A tumors had the lowest (1.012) and HER-2-enriched tumors the highest (1.286) mean ADC values (p = 0.02). The Bonferroni correction for multiple comparisons showed that only HER-2-enriched tumors had mean ADC values that were significantly different from those observed in the other subgroups.

Conclusions. We could not find an association between ADC values and single breast cancer histopathological features. However, mean ADC values resulted different according to breast cancer subtypes. This finding, which may have prognostic and therapeutic implications, deserves further investigation.