Results: Sixty two patients were included in the standard population, of which 38 received low-dose X, with an objective response rate of 42% (16/38), and 24 received standard-dose X, with a response rate of 54% (13/24). Median TTP was 151 and 140 days, respectively.
Conclusions: These results suggest that lower-dose X (1,000 mg/m^2 b.i.d.) has comparable efficacy to standard-dose X (1,250 mg/m^2 b.i.d.) when administered for $\geqslant$6 weeks to older patients with ABC.

5061 POSTER

Gemcitabine and carboplatin in heavily pretreated metastatic breast cancer: predictive value of breast cancer subtypes

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Background: Patients (pts) with breast cancer (BC) are increasingly exposed to anthracyclines and taxanes either as adjuvant treatment or during initial therapy of metastatic disease. This trial studied the efficacy and safety of gemcitabine and carboplatin (GC) in unfavorable subgroup of pts affected by heavily pretreated metastatic BC.
Patients and Methods: We included HER-2 negative metastatic BC refractory or resistant to previous anthracycline- and taxane-based chemotherapy, and HER-2 positive metastatic BC with at least two progressions of disease during protracted trastuzumab-based therapy. Other inclusion criteria were: age $\geqslant$18 years, ECOG PS of 0−2, RECIST-defined measurable MBC. Treatment consisted of gemcitabine (1000 mg/m^2 iv on days 1 and 8 and carboplatin (AUC 5 iv on day 1) applied every 3 weeks.
Results: Forty-two pts were registered. The 1-year disease control rate (PR + CR + SD) was 62%, with a median time to progression (TTP) of 7.0 mos (range 1−12 mos) and a median overall survival (OS) of 10.5 mos (range 1−34 mos). Overall, grade $\geqslant$3 toxicities included neutropenia (45%), and thrombocytopenia (7%). Other non-hematologic toxicities were irrelevant. We performed a subgroup analysis in order to evaluate the prognostic and predictive significance of immunohistochemically defined subsets of pts. According to the definition proposed by BCIRG trialists (Hugh J, et al. J Clin Oncol 2009; 27: 1168–1176), pts were grouped as triple negative (ER negative, PR negative, HER-2 negative), HER-2 (HER-2 positive, ER negative, PR negative), Luminal B (LB) (ER positive and/or PR positive and either HER-2 positive and/or Ki67^{high}), and Luminal A (LA) (ER positive and/or PR positive and HER-2 negative and Ki67^{low}). LA pts had lower 1-year disease control rate than other subtypes (LA 34% vs others 74%; Fisher's exact p = 0.02), shorter PFS (LA 2.4 mos vs others 6.3 mos, HR = 0.62; 95% CI = 0.28−1.39; Log-rank test p = 0.015), and shorter OS (LA 7.5 mos vs others 11.7 mos, HR = 0.52, 95% CI = 0.23−1.16; p = 0.034).
Conclusions: Chemotherapy with GC is an effective and generally well-tolerated treatment option for intensively pretreated pts with metastatic BC. Pts affected by LA subtype BC seem to fare poorly as compared to others subtypes. Specific gene-expression signature between LA and other subtypes might explain the different outcome.

5062 POSTER

Fulvestrant in heavily pre-treated ER-positive post-menopausal metastatic breast cancer patients: final update of a phase II study

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Background: Fulvestrant (F), an estrogen receptor down-regolator drug, is effective in ER +ve post-menopausal metastatic breast cancer (MBC) progressing on Tamoxifen (Howell A., 1995) and has demonstrated overall response rates (OORR), time to progression (TTP) and overall survival (OS) comparable with Anastrozole (Howell A., 2000 and Mauriac L., 2003). The aim of the study was to evaluate efficacy and toxicity of F in ER+ve post-menopausal metastatic breast cancer patients (pts) heavily pre-treated both with hormonal agents and chemotherapy.
Materials and Methods: From 5/2006 to 12/2008, F 250 mg i.m. q 28 days was administered to 27 ER+ve post-menopausal MBC pts, median age 64 (range 39−81). Fifteen pts (55.5%) had received prior chemotherapy for MBC, and all pts had received prior hormonal therapy (median 2 drugs: range 1−4). Metastatic sites were: 20 bone, 8 liver, 8 lung, 9 nodes, 5 skin, 5 breast. A total of 186 cycles of F were delivered, median 6 cycles/pt. (range 2−24). All pts were valuable for toxicity and for efficacy.
Results: Overall response rate (OORR) was 13.7% (0/27CR, 4/27PR) and stable disease (SD) was observed in 9 pts (33.3%); clinical benefit (OORR + SD) was obtained in 13/27 pts. (48.1%). Median TTP in all pts was 7+ mos (range 2−30+ mos.) and in pts obtaining clinical benefit was 9+ mos (range 4−30+ mos). Median OS was 14 mos. (range 3−41+ mos) and 20 mos. (range 9−41+) in pts obtaining clinical benefit. No G3−4 toxicities were observed: G1−2 coetaneous rash occurred in 3/27 (11.1%) pts. and G1−2 asthenia in 3/27 (11.1%) pts.
Conclusions: This phase II study demonstrated that F is safe and effective in heavily pre-treated ER+ve post-menopausal MBC pts. Results from this phase II trial are comparable with those observed in pivotal trials, when F was used as 2nd line treatment, suggesting F has comparable efficacy in heavily pretreated MBC pts.

5063 POSTER

Paclitaxel combined with ifosfamide in anthracycline- and docetaxel-pretreated metastatic breast cancer

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Background: The aim of this study was to evaluate the efficacy and tolerability of paclitaxel and ifosfamide in anthracycline-/docetaxel-pretreated breast cancer.
Materials: Advanced breast cancer patients who had received prior anthracycline- and docetaxel-based chemotherapy were eligible. Paclitaxel (175 mg/m^2 i.v. in a 3-hour infusion) on day 1 and ifosfamide (1.5 g/m^2 i.v. in a 15-min infusion) on days 1−3 were given every 3 weeks for a maximum of 9 cycles. Tumor response was assessed by using RECIST criteria every 2 cycles.
Results: Thirty-four patients (33 with metastatic and 1 with locoregional disease) were enrolled. Anthracycline- and docetaxel-based chemotherapy were previously given to 1/17/13 and 1/12/21 patients in neoadjuvant/adjuvant/metastatic settings, respectively. Three patients did not previously receive anthracycline due to abnormal cardiac function. The response rate under the intent-to-treat analysis was 27.6% (8/34; all partial responses) with the median response duration of 14 months. The median disease control rate was 70.6%. The median progression-free and overall survival was 5.9 and 8.5 months, respectively. A total of 174 cycles of chemotherapy were delivered with median 6 cycles. In terms of toxicities, grade III/IV neutropenia was 46.6% (81/174 cycles) with febrile neutropenia of only 1.7% (3/174 cycles). Grade III/IV nonhematological toxicities were peripheral neuropathy (17.6%; 6/34 patients), infection (11.8%; 4/34 patients) and liver enzyme elevation (2.9%; 1/34 patients). There was one treatment-related death from sepsis.
Conclusions: Paclitaxel combined with ifosfamide was effective and tolerable in anthracycline-/docetaxel-pretreated advanced breast cancer. Overcoming docetaxel resistance by using paclitaxel in combination with ifosfamide needs to be addressed via further investigation.

5064 POSTER

Zoledronic acid in breast cancer patients with bone metastasis

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Background: Zoledronic acid is a nitrogen containing bisphosphonate that has been proven to reduce oestoprosis and cancer induced osteolysis. Zometa has been the treatment of choice for the prevention of skeletal complication of bone metastasis (pain, pathological fracture) in patients with breast cancer, which have a significant impact on the quality of life of patients. The aim of the study is to evaluate the efficacy and tolerability of Zometa in improving pain scores and quality of life in patients with bone metastasis secondary to breast cancer.
Material & Methods: 150 patients with bone metastasis and pathologically confirmed carcinoma of the breast during the period between January 2004 and January 2006 were enrolled, ECOG PS 0−2, and adequate renal function. Treatment consisted of Zometa 4 mg IV over 15 minutes repeated every 3−4 weeks concurrently with chemotherapy and/or hormonal therapy or radiotherapy if treatment was needed. Zometa administered continuously until impairment in the performance status, progression of the disease or severe adverse events. Pain was evaluated by present pain intensity from McGill Melzack (PPI) questionnaire, quality of life (QOL) was assessed with functional assessment of cancer therapy (FACT) questionnaire.
Results: The median age was 48 years (range 30−65 years), median PS 1, extent of disease (metastasis): 60 patients (40%) had only one bone

metastatic site & 30 patients (20%) had more than 3 bone metastatic sites. The average number of administered cycles were 12 (range 6−50) and the average accumulated dose was 48 mg (24–200 mg). 75 patients (50%) received treatment continuously for two years. The calcium and creatinine serum level were assessed before each infusion. A total of 5 patients (3.3%) developed hypocalcemia (Ca <8 mg/dL) and 2 patients (1.3%) experienced an increase in serum creatinine (>8 mg/dL), twelve patients (8%) had an increase of pain after the first infusion of Zometa, the rate of objective reduction in pain with Zometa was 48% of patients after 6 infusion. The improvement of quality of life occurred in 75 patients (50%).
Conclusion: Zometa significantly improves the QOL and pain score. It can be administered simultaneously with chemotherapy, hormonal therapy, and radiotherapy without relevant clinical problems.

5065 POSTER

Metronomic weekly use of zoledronic acid for breast cancer with bone metastases has more potent antitumor and bone-preserving effects than conventional zoledronic acid given every-four-weeks

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Background: Zoledronic acid (ZOL) has direct and indirect antitumor effects, however, the pharmacokinetics of the drug in breast cancer patients remain to be elucidated and optimized. The main study objectives were to compare the effects of ZOL on bone resorption, angiogenesis, tumor markers and time to disease progression between a weekly low dose (the metronomic regimen) versus a conventional dosage.
Materials and Methods: Sixty breast cancer patients with bone metastases were recruited to a randomized phase II trial. They were randomized to either ZOL 1 mg IV weekly for 4 doses or a single dose of ZOL 4 mg IV. No other antitumor treatments were administered during the first month after randomization. Serial blood samples were collected on day 1, 15 and 29 to measure markers for bone resorption (N-telopeptide), angiogenesis (VEGF) and tumor burden (CEA and CA15−3).
Results: Compared to a single-dose administration, weekly low-dose of ZOL resulted within the first 4 weeks in significantly greater reductions in serum levels of VEGF and N-telopeptide, with more reduction towards the end of the first month of treatment. Compared with baseline serum VEGF levels, the percentages of more than 25% reduction with the metronomic regimen were 50% and 96.6% on day 15 and 29, respectively, while the corresponding values with conventional dosing were 23.3% and 17.2%, respectively. Patients who received metronomic ZOL had a substantially longer median TTP (7.0 months, 95%CI, 6.1−7.9 months) than those who had a single dose of ZOL (2.8 months, 95%CI, 0−5.7 months; P = 0.076).
Conclusions: Metronomic use of low-dose ZOL appeared to be more effective than conventional regimen in sustained reduction of circulating VEGF and N-telopeptide levels, and in prolonging TTP. This dosing schedule should be further assessed in phase III trials.
(ClinicalTrials.gov number, NCT00524849)

5066 POSTER

Nab-paclitaxel weekly or Q3w compared to docetaxel Q3w as first-line therapy in patients with metastatic breast cancer (MBC): an economic analysis of a prospective randomized trial from the perspective of the German health care system

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Background: In patients with MBC, a common practice in Germany is first-line chemotherapy with a taxane, usually docetaxel. However, docetaxel is associated with dose-limiting toxicity often requiring dose reductions, delays and in some cases prophylactic hematopoietic growth factors. A nanoparticle albumin-bound (*nab*) formulation of paclitaxel (Abraxane™) was recently developed to overcome the safety drawbacks of docetaxel and to provide additional efficacy. A randomized phase II trial comparing *nab*-paclitaxel 100 or 150 mg/m^2 weekly 3 out of 4 and *nab*-paclitaxel 300 mg/m^2 q3w to docetaxel 100 mg/m^2 q3w reported improved progression-free survival and reduced toxicity with the former regimens (Gradishar, 2009). To measure the economic value of the *nab*-paclitaxel regimens in Germany, an economic analysis was conducted.
Methods: The current study extracted data captured during the randomized trial (Gradishar, 2009). Resource utilization data contained within the database were converted into German cost estimates. This consisted of costs for chemotherapy, drug delivery, monitoring, supportive care drugs, and hospitalization due to toxicity. Univariate and multivariate regression analysis was then conducted to compare the total cost of therapy in patients randomized to each of the four regimens.
Results: Hematopoietic growth factor use, hospital days for side effects management, and toxicity-induced protocol discontinuations were higher in the docetaxel group. When all of the cost components were combined for the entire population (n = 300), patients in the *nab*-paclitaxel 100 mg/m^2 weekly and 300 mg/m^2 q3w groups had comparable costs to the docetaxel control (€18,057 vs. €19,236 vs. €16,370; p = NS). The *nab*-paclitaxel 150 mg/m^2 weekly arm had significantly higher overall costs of €31,184 but was associated with an improvement in progression-free survival relative to docetaxel. As alternatives to docetaxel, the incremental cost per progression free year gained with *nab*-paclitaxel 100, 150 mg/m^2 weekly and 300 mg/m^2 q3w were €3,800, €32,900 and €9,800 respectively.
Conclusions: Given its more favorable safety profile, superior efficacy, and comparable economic impact, *nab*-paclitaxel (weekly or q3w) can be considered a preferred option over docetaxel as first-line chemotherapy in MBC from the perspective of the German health care system.

5067 POSTER

Increased overall response rate to capecitabine in different patient subgroups: results of an open-label phase II study in pretreated metastatic breast cancer

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Background: Capecitabine (X) has demonstrated high efficacy in patients with metastatic breast cancer (MBC) pretreated with anthracyclines and taxanes. Study M66103, an open-label phase II study, investigated the activity and tolerability of X in MBC after pretreatment with paclitaxel or docetaxel. The primary endpoint was overall response rate (ORR); here we report ORR in different patient subgroups.
Methods: 136 patients received X (1,250 mg/m^2 b.i.d. for 14 days followed by 7 days' rest). The median age was 56 years (range 32−77); median KPS 90% (range 60–100); median number of metastatic sites 2 (range 1−8), most commonly liver (53%) and bone (42%). Patients had received a median 2 prior regimens (range 1−6); 99% of patients had received taxane-containing therapy; 49% paclitaxel, 46% docetaxel; 4% both paclitaxel and docetaxel; 93% an anthracycline; and 52% a 5-FU-containing regimen.
Results: ORR was 16% (95% CI: 10−23%), including 2 complete and 20 partial responses, while 62 patients (46%) achieved stable disease for a tumour control rate of 62% (95% CI: 53−70%). Analysis by patient subgroup revealed a significant impact on ORR for: baseline Bloom-Richardson histological grading 2 vs 3 (ORR 26.2% vs 9.5%, p < 0.05); baseline laboratory values: thrombocytes value 0 or 1 ($\leqslant 350 \times 10^6$ g/L) (ORR 3.1% vs 20.2%, respectively, p = 0.025) and carcinoembryonic antigen value 0 or 1 (>25 μg/L) (ORR 6.0% vs 25.0%, respectively, p = 0.027). A trend towards improved ORR was noted in patients with liver metastases vs no liver metastases (ORR 21.9% vs 10%, p = 0.06). Other baseline characteristics had no impact on ORR: age; performance status; TNM state, hormone receptor status, disease-free interval, interval between diagnosis and study start, number of metastatic sites, study centre, previous therapy, and other baseline laboratory values (haemoglobin, white blood cells, carbohydrate antigen 15−3, alkaline phosphatase). Most treatment-related adverse events (AEs) were mild to moderate: 35 patients reported grade 3/4 toxicity. The most common grade 3/4 AEs were hand-foot syndrome (11%), diarrhoea (7%), vomiting (4%), and nausea (3%).
Conclusions: These data confirm that X is an active and well-tolerated treatment for pretreated MBC, with different patient subgroups showing increased ORR. The high tumour control rate and ease of administration provide an effective and convenient treatment approach in this patient group.