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.