in comparison to serum HER2/neu positive patients (mean: 31.3 weeks; p=0.018).

Conclusions: Our results indicate that an elevated serum HER2/neu level is a negative predictive factor for bad treatment outcome in terms of progression-free survival. This result, together with the putatively increased anthracycline sensitivity of HER2/neu positive patients, may help for patient selection to a more individualized mode of chemotherapy.

719 POSTER

Biological study of anastrozole in post-menopausal advanced breast cancer (ABC) patients: Effects on bone metabolism and oestrogen suppression

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Purpose: To study the short term biological effect of anastrozole on serum oestrogens, androgens, 17OH-progesterone (17OH-PGR), gonadotrophins, sex hormone binding globulin (SHBG) and bone metabolism markers.

Methods: 34 consecutive pts with ABC received anastrozole 1 mg/day treatment Blood samples were taken before and at 2, 4, 8 and 12 weeks during treatment to measure serum levels of: oestrogens (E1, E2 and E1-S), androgens (Δ4, DHT, TST, Free TST, DHEA and DHEA-S), 17OH-PGR, SHBG and gonadotrophins. As indicator of bone resorption we measured serum carbossi-terminal telopeptide of type I collagen (ICTP) and the cross-linked N-telopeptide of type I collagen (NTx), and for the osteoblastic activity intact osteocalcin (BGP) and bone alkalyne phosphatase (BAP).

Results: After 2 weeks E_1 and E_1-S levels decreased of an average of 56% (range 23.1–88.8) and 75.8% (range 52.4–87.2) respectively; E_2 decreased of an average of 62% (range 31.4–89.6). No significant changes were detected in androgens and 17OH-PGR. There was a significant increase of gonadotrophins over time ($p = 0.0001$ and $p = 0.0001$ for LH and FSH, respectively), and a significant decrease in SHBG $p = 0.0001$. A progressive significant increase in bone metabolism serum markers was detected in all pts: $p = 0.0394$ for BAP, $p = 0.0156$ for BGP, $p = 0.0021$ for ICTP and $p = 0.0013$ for NTx. In particular, pts with bone metastases had an increase statistically significant of bone resorption markers ($p = 0.0019$ for ICTP and $p = 0.0251$ for NTx) and borderline for bone formation markers. In pts without bone disease BAP, BGP and ICTP remained unchanged, whereas serum NTx significantly increased $p = 0.0186$.

Conclusion: Anastrozole is a selective aromatase inhibitor as it does not modify serum levels of androgens and 17OH-PGR. In our experience no relation was found in the short term period between serum oestrogen suppression and bone metabolism. The evaluation of bone metabolism markers seems to be helpful for the monitoring of bone disease during hormonal treatment.

720 POSTER

Safety and activity of Capecitabine in elderly patients with advanced breast cancer

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Purpose: Capecitabine is a selectively tumor activated fluoropyrimidine which is effective in a wide range of solid tumors. This study tested the safety and the activity of Capecitabine in elderly patients (pts) with advanced breast cancer (ABC).

Methods: From May 1999 to March 2001 forty consecutive pts were treated. The first thirty pts were treated using a dosage of 2500 mg/sqm/day b.i.d. for 2 weeks with a week of rest; than to improve the safety profile we are continuing the trial by reducing the dosage (2000 mg/sqm/day). The pts median age was 74 years (range 65–89). Pts could receive one prior chemotherapy and/or 2 hormonal regimens for metastatic disease. A previous therapy containing 5-fluorouracil was allowed but a 12 months withdrawal period was required, starting from the last dosage of the previous treatment. The metastatic sites were liver (19), lung (14), soft tissue (12), bone (9), other (9).

Results: Toxicity according to NCI-CTC Bethesda was: *grade 3–4* diarrhea (10%), *grade 3* vomiting (7%), *grade 2* (10%) and *grade 1* (26%) hand-foot syndrome, *grade 2–3* asthenia (13%), *grade 2* stomatitis (7%). One patient died for gastrointestinal toxicity and one patient developed deep venous thrombosis. The objective responses were 11/31 (35%), 3% complete remission, stabilizations of disease were 9/31 (29%), and progressions 11/31 (35%). The median time to progression was 6 months.

Conclusions: These results suggest that Capecitabine is safe and active in elderly pts with advanced breast cancer.

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721 POSTER

Paclitaxel-ifosfamide for anthracycline-resistant advanced breast cancer

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The combination of paclitaxel 135mg/m2 as a 3 hour infusion on day 1 and ifosfamide 1.7 g/m2 as a 4 hour infusion on days 2 to 4 every 22 days was given to patients (pts) with advanced breast cancer resistant to anthracyline containing regimen or patients relapsed after antracycline containing adjuvant chemotherapy. Pts had to have measurable or evaluable progressive metastases or local disease, and only one regimen for metastatic disease. Thirty one pts with a median age of 49 years (range, 30-69) entered the study. Nine (29%) had lung and seventeen (55%) liver metastases (mts), nineteen (61%) bone mts. Only seven (23%) had lymph node mts and four (13%) skin mts. Median of 7 cycles (range 1-18) were delivered. Responses were evaluated according to WHO guidelines and side effect according to NCI criteria. A panel of oncologist and one radiologist reviewed all responses. At baseline only three patients (10%) were free of the adverse consequenses of the prior therapy. During the treatment severe toxicities (grade >3) included nausea 3%, vomiting 3%, pulmonary 3%, neuromotor 3%, asthenia/fatigue 7%, pain 7%, neutropenia 90%, thrombocytopenia 10%, anaemia 10%, infection 7%, while alopecia was universal. Three complete responses (10%), 10 partial responses (32%), 8 (32%) stable disease and 8 progressive disease (26%) were documented. Median survival and progression free survivals after beginning of treatment were 19.3 months and 6.1 months, respectively.

Conclusion: Combination of paclitaxel and ifosfamide seems to be a promising regimen (objective response rate of 42% and a median survival time of 19 months) with acceptable side effects in advanced breast cancer patients relapsed after antracycline based adjuvant treatment or resistant to antracycline treatment.

722 POSTER

Salvage treatment with irinotecan and gemcitabine in breast cancer patients pretreated with taxanes and anthracyclines: a multicenter phase II study

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Purpose: A multicenter phase II study was conducted to evaluate the efficacy and toxicity of the irinotecan (I) - gemcitabine (G) combination in women with disease progression after initial chemotherapy for metastatic breast cancer.

Patients and Methods: Thirty-six breast cancer patients pretreated with regimens including taxanes and anthracyclines received G 1200 mg/m2 on day 1 and day 8 and I 300 mg/m2 on day 8, every 3 weeks. The median age was 58 years and the performance status (WHO) was 0-1 in 26 (72%) patients and 2 in 10 (28%). Nineteen patients had received one, and 17 two or more prior chemotherapy regimens.

Results: All patients were evaluable for toxicity and 28 for response. One-hundred forty treatment cycles were administered with a median of 3.5 cycles/patient. Complete remission was recorded in one (4%) patient and partial response in 5 (18%) for an overall response rate of 22% (95% CI: 6.23% - 36.63%). Nine (32%) patients had stable disease and 13 (46%) progressed. Responses were observed at all metastatic sites with a median duration of response of 5.5 months (range, 2.5 to 6.5), and a median time to progression of 7.5 months (range, 4.5 to 15.5). The median survival was 9 months (range, 1 to 13) and the one-year survival rate 37%. Grade 3 neutropenia occurred in 7 (19%) and grade 4 in 6 (17%) patients. Neutropenia was associated with fever in 3 (9%) patients without toxic deaths. Grade 3 thrombocytopenia developed in 4 (11%) patients and grade 4 in 1 (3%). Non-hematologic toxicity was mild with grade 2-3 diarrhea reported in 6 (17%) patients and grade 2-3 asthenia in 13 (35%).