**254** POSTER

**Trastuzumab and Vinorelbine combination in the treatment of metastatic breast cancer**

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Trastuzumab and Vinorelbine combination has previously shown a very interesting activity and is a well tolerated regimen in metastatic breast cancer overexpressing Her2. From February 2001 to August 2003, 46 patients (pts) have been treated with this combination in 13 Spanish centers. The primary endpoint of the study was response rate and secondary objectives were TTP and to define the toxicity profile of the combination in this setting. Pts without previous treatment for metastatic disease or after first line therapy were included in this study. Only Her2 3+ or 2+ confirmed by FISH were eligible patients. Patients were treated with weekly Trastuzumab given at a dose of 2 mg/kg/d over 30′ (4 mg/kg/d over 90′ on the first infusion) followed by Vinorelbine at a dose of 25 mg/m2 over 6–10′.

**Material and Methods:** 46 female patients with measurable or assessable metastatic breast cancer were enroled. Patients remained in study up to six cycles consisting of 3 administrations of the combination and then up to the investigator some pts went on Herceptin alone or other CT regimen. All pts were followed until progression of the disease. Response assessments were scheduled after 2, 4 and 6th cycles.

**Results:** 29 pts had not received any treatment for metastatic disease and 17 had received one or more lines of treatment for metastatic disease. We have actually data from 41 pts evaluable for response. So far, the overall response rate is 66%. 7 pts have shown a CR (17%), 20 had a PR (49%), 7 had a EE (17%) and 7 had a PD (17%) as the best response to therapy. Toxicities led to study termination in only 1 pts, being G1–2 neurotoxicity and G3–4 neutropenia main toxicities. No cardiac events have been seen in this group of pts. No SAEs have been reported.

**Conclusions:** This regimen shows a remarkable activity with a good tolerance which should be taken under consideration while treating patients in this setting. Further data of the full cohort of patients will be presented at the meeting.

**255** POSTER

**Long-term (4-year) safety of intravenous ibandronate in metastatic breast cancer: an open-label study**

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**Background:** Certain intravenous bisphosphonates for metastatic bone disease (zoledronic acid and pamidronate) have been linked to renal toxicity, with evidence to suggest that it may be caused by drug accumulation when receiving long-term therapy [1,2]. However, a 96-week, phase III clinical trial demonstrated that intravenous ibandronate 6 mg infused every 3–4 weeks has a renal safety profile that is similar to placebo in patients with bone metastases from breast cancer [3]. In order to better assess the renal adverse event (AE) profile and investigate the possibility of renal toxicity with drug accumulation, this abstract reports 4-year follow-up data from this trial.

**Methods:** Patients completing the placebo-controlled trial period were entered into a 2-year non-controlled study, in which intravenous ibandronate 6 mg was infused over 1–2 hours every 4 weeks (n=62). AEs and laboratory signs were recorded.

**Results:** As expected with advanced malignant disease, 10% of patients did not complete the 2-year follow-up period due to AEs, and the majority of patients (77%) experienced at least one AE. Disease progression accounted for 44% of all reported AEs. Serious AEs affected 26% of patients, but were not drug-related. The most common treatment-related AE was gastroenteritis, which affected just two patients. There were no clinically-relevant renal AEs or laboratory abnormalities.

**Conclusions:** Ibandronate has been shown to be effective and well-tolerated in 2-year placebo-controlled trials. This study demonstrates that intravenous ibandronate 6 mg has a favorable tolerability profile over 4 years of treatment, with no renal safety concerns. These results suggest that there is no renal toxicity accumulation issue with ibandronate. The long-term safety of intravenous ibandronate may reduce the time and cost burden associated with regular renal function monitoring (not required prior to each dose) and the management of drug-related AEs.

**References**

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**256** POSTER

**Is the response duration to aromatase inhibitor anastrozole in metastatic breast cancer correlated with Her-2/neu status? Preliminary results of a prospective, non-randomized study**

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**Background:** The aromatase inhibitor anastrozole is effective in metastatic breast cancer (mbc) in patients (pts) with ER/PgR positive tumors, both in first-line treatment and in pts pretreated with tamoxifen (Tam). Several data suggests the potential correlation beetwen Her-2 expression and benefit from hormonal treatment. Therefore, we performed a prospective, non-randomized trial of correlation with Her-2/neu status and the response duration (RD) to anastrozole in mbc.

**Material and Methods:** 35 postmenopausal, steroid receptors positive pts with metastatic disease were eligilible. 17 tumors were ER positive, 18 were both ER/PgR positive. 29 pts were pretreated with Tam as an adjuvant (14) or metastatic disease (15). 15 pts were previous treated with chemotherapy (chth) because of mbc. Median of number cycles chth was 1. In 8 pts anastrozole was the first-line therapy of mbc. Median of number metastatic sites was 2. Retrospectively Her-2/neu status was indicated (in 33 specimens by immunohistochemy DAKO test, in 2 specimens by FISH). In 19 tumors Her-2 were negative, in 10 Her-2 overexpression was confirmed, in 6 specimens Her-2 expression was evaluated on 2+ and in these cases FISH tests should be performed. The endpoint of this study is the duration response and time to progression (TTP) on anastrozole in Her-2 overexpressors to Her-2 nonoverexpressors.

**Results:** The median response duration (mRD) was 26 weeks in Her-2 positive and 30 weeks in Her-2 negative pts but without statistically significance. There were 7 cases (70%) of progression in Her-2 positive group with TTP 22 weeks and 7 (39%) cases of progression in Her-2 negative group with TTP 14 weeks. In the group with Her-2 status 2+ mRD was 20 weeks and in all cases progression was observed with mTTP 20 weeks. In this group FISH tests will be performed and results will be included to this analysis.

**Conclusions:** There is no significant differences in the response duration and time to progression in pts with mbc treated with anastrozole in dependence of Her-2 status in analysed group. Observations are not closed yet and new pts are included to the study. Final results will be presented in a few years time.

**257** POSTER

**Navelbine® (NVB) alternating oral and i.v. plus epirubicin (EPI) as first line chemotherapy of metastatic breast cancer (MBC): phase II study – final results**

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The combination of NVB IV 25 mg/m$^2$ on days 1 and 8 and EPI 90 mg/m$^2$ on day 1 every 3 weeks is an effective option for the first line treatment of MBC. In an effort to improve patient convenience, the day 8 administration of NVB was given orally at the dose of 60 mg/m$^2$ while NVB IV was used the day of EPI infusion. This study evaluated efficacy and tolerance of this new combination given for 6 cycles. Prior adjuvant chemotherapy completed at least 12 months before study entry was allowed with cumulative doses up to 180 mg/m$^2$ of doxorubicin, 360 mg/m$^2$ EPI and 72 mg/m$^2$ mitoxantrone. Patients had measurable disease (WHO criteria), normal LVEF and PS 0–1 at study entry. The characteristics of the 49 patients treated, were median age of 55 yrs, prior adjuvant chemotherapy in 51%, prior adjuvant hormonotherapy in 57.1%, disease free interval <2 years in 32.7%, visceral involvement in 81.6%