No serious renal disorders or ONJ cases were reported during this time frame. Overall, the incidence of adverse events was not different between the two arms.
Conclusion: This geographically diverse study confirms the effectiveness of the zoledronic acid to prevent AIBL as documented in the North American Z-FAST study and the rest of world study, ZO-FAST.

2009 POSTER

Safety of the combination of lapatinib (L) plus trastuzumab (T) in patients (pts) with HER2-Positive (+) metastatic breast cancer (MBC)

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Background: L, an oral, dual EGFR/HER2 tyrosine kinase inhibitor, and T, a humanized anti-HER2 antibody, are approved in HER2+ MBC. Based on preclinical synergy and different mechanisms of action, L+T was studied in HER2+ MBC. Data from 4 trials were analyzed to assess safety of L+T.
Methods: From July 2003 to Mar 2007, 393 women of median age 51 years (range: 22−81 years) with HER2+ MBC received L±T (n = 351) or L+T+ paclitaxel or docetaxel (n = 42). L dose range: 500–1500 mg/day; 297 pts received ⩾1000 mg. T dose: 2 mg/kg/week. Drug-related adverse events (AE) graded by NCI CTCAE were analyzed. Cardiac function (LVEF) was assessed at screening, 8 weekly after starting L+T, and at withdrawal via MUGA or echocardiogram. Rate of symptomatic cardiac events (CE; CTCAE Grade 3/4 LV systolic dysfunction) or asymptomatic LVEF decreases (⩾20% relative to baseline and below institution's lower limit of normal) were assessed.
Results: Common drug-related AEs were diarrhea (53%), rash (25%), nausea (24%), fatigue (19%), and vomiting (13%). Maximum grade (G) reported by most was G1 or G2. G3 AE rate was ⩽3% except diarrhea in 12% (including G4 in <1%). Eight pts had single asymptomatic LVEF decreases, 2 had 2 asymptomatic decreases, and 2 (0.5%) had symptomatic CEs, totaling 14 decreases in 12 (3.1%) pts. Pts received prior T± anthracyclines (A; n = 8), A (n = 2), or unknown therapy (n = 2). For asymptomatic events, mean baseline and nadir LVEFs were 65.3% (range: 58−74%) and 46.1% (range: 42.5−51%), respectively. Mean absolute decrease was 19.4% points (range: 13−29%). Median time to onset and duration of LVEF decrease was 55 (range: 18–282) and 9 days (range: 4–113), respectively. L+T was interrupted in 4 pts and continued in 4 despite LVEF decrease. Two events occurred after L was discontinued. Asymptomatic LVEF decrease resolved without sequelae in 7 pts, unresolved in 2, ongoing at death (disease progression) in 1. Two pts had symptomatic CEs (LVEF 58% to 25% and 69% to 25%) after 365 and 42 days of L+T, respectively. L+T was discontinued in both; 1 recovered after 17 days and 1 died (cardiac insufficiency/pulmonary thromboembolism).
Conclusion: Preliminary data indicate L+T was well tolerated in pts with HER2+ MBC. Rates of drug-related AEs were consistent with those reported for L and T alone. Combined HER2 inhibition with L+T does not unexpectedly increase the risk of CE. L+T is currently being studied in neoadjuvant and adjuvant trials in HER2+ BC.

2010 POSTER

Comparative analysis of circulating tumor cells (CTCs) in peripheral blood and disseminated tumor cells in the bone marrow (DTC-BM) of breast cancer patients

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Background: The detection of Disseminated Tumor Cells in the Bone Marrow (DTC-BM) of breast cancer patients is an independent prognostic factor in all stages of the disease. As less invasive procedure the analysis of Circulating Tumor Cells (CTCs) in Peripheral Blood (PB) could be an alternative especially for repeated follow up examinations. Automated systems und molecular methods (PCR) could increase sensitivity and offer the possibility of further characterizations of those cells.
Methods: BM aspiration and blood draw is performed simultaneously. Immunocytochemical examination of DTC-BM with the anti-Cytokeratin (CK) antibody A45B/B3 follows a standardized protocol. Analysis of PB (7.5 ml) for the presence of CTCs is performed with the CellTracks Analyzer system (Veridex, NJ, USA). After immunomagnetic enrichment by anti-Epcam antibodies CTCs are stained against CK, CD 45, and, optionally, HER2 by immunofluorescence. Positive events are recognized automatedly and presented on a screen for evaluation.
Results: Up to now, comparison of BM and PB of 44 patients could be performed. DTC-BM and CTCs in PB were detected in 15/44 (34%) cases each. Overall congruence of positive and negative findings was 68% (p = 0.05). 32 pts were examined at primary diagnosis. Of those, 19 (59%) showed both negative BM and PB, 6 (19%) DTC-BM (1−11) with negative PB, 6 (19%) CTCs (2–123) with negative BM, and 1 (3%) both. Patients with presence of CTCs at primary diagnosis tended to have higher tumor stage (T2-T4), Grading 2/3, 4 presented with lymph node metastases. Of 6 patients at recurrence free follow up examination, 3 had both positive BM and PB and 3 both negative status (100% congruence). Of the 6 pts with distant metastases, 5 showed DTC-BM (1–>1000) and 5 CTCs (2−77), all 4 patients with visceral metastases both.
Conclusion: If our results can be confirmed in a larger series, examination of CTCs in PB could add valuable information and allow monitoring of the disease during follow up. Further characterization of CTCs might enable risk stratification and application of targeted therapies. Aim of our ongoing research is the detection and characterization of CTCs by rt-PCR for tumor specific mRNA.

2011 POSTER

Serum BCL-2 and VEGF in women with breast cancer – can they detect the recurrence before CEA and CA15−3?

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Purpose: The purpose of our study is to investigate if serum VEGF and bcl-2 can be used as prognostic factors during the follow-up of the patients with breast cancer and to compare these two factors with CEA and CA15−3.
Patients and Methods: 200 patients with breast cancer stage I and II are enrolled in our study. The mean age of the patients was 59.65±11.65 years. 102 patients had quadrectomy and axillary lymph node dissection and 98 had mastectomy. After the surgical treatment they had supplementary therapy. The size of the tumor was <2 cm in 105 patients and >2 cm in 95 patients. The histological type was ductal carcinoma in 169 patients, lobular in 10 and DCIS in 2 patients. 54 patients had <3 lymph node positive, 46 had >3 positive lymph node and 100 had negative lymph node. 14 patients had recurrence of the disease after the 18 months of the surgical treatment. We measured serum VEGF and bcl-2 before and after the operation and the first and second year of their follow-up with ELISA. CEA and CA15−3 were measured every 4 months after the surgical treatment until the two years. The results have been analysed with curves ROC and Pearson method to find if VEGF and bcl-2 can be used during the follow up of the patients to investigate the recurrence of the disease before the clinical appearance. Also we examine if they can detect the recurrence earlier of CEA and CA15−3.
Results: After the analysis with ROC curves we found that bcl-2 can detect the recurrence of breast cancer preoperative (p = 0.066) and also postoperative (p = 0.037) and at second year (p = 0.029) of the follow-up of the patients. VEGF can detect the recurrence after the operation (p = 0.003). On the other side CEA can detect the recurrence in 20 months after the operation (p = 0.098) and CA15−3 in 8 (p = 0.045). There was no correlation with the size of the tumor, the histological type and the lymph node status.
Conclusion: These results shows that bcl-2 and VEGF in serum can be used in the follow-up of the patients with breast cancer as they can detect the recurrence of the disease much earlier of the clinical appearance. CEA and CA15−3 can also detect the recurrence before the clinical appearance but later of the other two factors. Serum bcl-2 is the most significant factor as it can detect the recurrence in three measurements.

Poster presentations (Mon, 24 Sep, 14.00−17.00)
Breast cancer – pre-clinical science

2012 POSTER

Activity of capecitabine (C) and docetaxel (D) doublets with and without trastuzumab (T) in a breast cancer xenograft model

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Background: In the setting of pretreated metastatic breast cancer, C is highly active, well tolerated, and extends survival when D is added to C. Preclinical data on C+D doublets ± T, a humanized monoclonal antibody