On average, E2 concentrations relative to entry, were half that with A than with F at 2 and 4 weeks (21% of entry value with A and 42% of entry value with F). E1 and E1S were analysed by a new iodinated radioimmunoassay after column chromatography, and will be reported in detail.

PP-8-6 Paclitaxel (P) Versus Doxorubicin (D) as First Line Chemotherapy (CT) in Advanced Breast Cancer (ABC): A Randomized Trial with Crossover of the EORTC-IDBBC in Collaboration with EORTC-ECSG

P. Bruning*, M.J. Piccart, J. Klijn, T. Gamucci, Z. Kusenda, J.A. Roy, A. Van Vreckem, R. Paridaens, IDBBC.

This trial was designed to investigate the efficacy and safety of P (200 mg/m^2, 3 H infusion, q3w) with crossover to D (75 mg/m^2, q3w) on progression, versus the reverse sequence. Crossover is mandatory if progression occurs within the first seven cycles of first-line CT. Until now, a total of 316 pts have been randomized (expected: 330 pts). Preliminary results on toxicity have been presented (ECCO8). An attempt to correlate some patient/disease characteristics (as possible predictors) with toxicity is ongoing. The following table summarizes the announced best response for pts of first and second line.

Response	Complete (%)	Partial (%)	Stable (%)	Progression (%)
1st line (n = 187)	4	34	27	26
2nd line (n = 49)	2	39	23	18

The intermediate results show a clearcut response rate in 2nd line with both drugs supporting a lack of cross resistance between P and D. An update on toxicity and antitumor activity will be presented.

PP-8-7 Assessment of Response in Bone within an EORTC Randomised Trial of Bisphosphonate Treatment (10924)

J. Vinholes*, R. Coleman, D. Lacombe, F. Mignolet, C. Rose, R. Leonard, J. Nortier, M. Tuibiana-Hulin, EORTC Breast Group.

Assessment of response in bone is currently based on the changes seen on serial plain radiographs. We have prospectively evaluated new biochemical markers of bone resorption including the urinary excretion of peptide-bound N-telopeptide (Ntx) and C-telopeptide (Crosslaps) fragments of type 1 collagen, free deoxypyridinoline (Fdpd), tumour marker levels, the EORTC quality of life QLQ-C30 questionnaire, and a pain score assessing the intensity of pain, analgesic consumption and performance status. 91 patients with newly diagnosed, radiologically confirmed metastatic bone disease were recruited to a placebo-controlled clinical trial designed to evaluate the contribution of oral pamidronate 300 mg daily to standard anticancer treatment. A bone scan and skeletal survey was performed before trial entry and X-rays of involved sites repeated every 3 months and at each change of systemic therapy or skeletal-related event. The biochemical, subjective and quality of life changes are to be correlated with the UICC response in bone to endocrine (n = 51) and chemotherapy (n = 33) both with and without concomitant oral pamidronate.

PP-8-8 Reduction of Skeletal Related Complications in Breast Cancer Patients with Osteolytic Bone Metastases Receiving Hormone Therapy, by Monthly Pamidronate Sodium (AREDIA®) Infusion

R. Theriault, A. Lipton, R. Leff, S. Gluck, J. Stewart, S. Costello, J. Simeone, J. Seaman, R. Knight, M. Heffernan, D. Reitsma*. *Houston, TX; Hershey, PA; Atlanta, GA; Sudbury, Canada; Waratah, Australia; Dunedin, New Zealand; Boston, MA; CIBA-GEIGY, Summit, N.J.*

182 patients receiving endocrine therapy for metastatic breast ca. (with at least one lytic lesion $\geq$ 1 cm) were treated with pamidronate disodium (Aredia) 90 mg infusion over 2 hrs every month $\times$ 12 and 190 patients received placebo. Skeletal related event (SRE) including pathologic fracture, cord compression, surgery and radiation therapy were primary endpoints. The overall skeletal morbidity rate (#SRE/year) was significantly lower for the pamidronate group when compared to the placebo patients (2.4 vs 3.6; p = 0.03). The time to first SRE was 10.9 months in the pamidronate group vs 6.9 months in the placebo arm. Fewer patients treated with pamidronate required radiation to bone (39 vs 63 placebo: p = 0.01). The time to first bone radiation was significantly longer in the pamidronate group (p = 0.005). Fewer pathologic fractures were seen in the patients who received the bisphosphonate (66 v. 83 placebo: p = 0.13). Among the patients with pain at baseline, pain scores decreased for the pamidronate group from baseline while they increased on placebo (p = 0.009). Significantly fewer pamidronate (30%) than placebo patients (43%) had an increase in analgesic use from baseline (p = 0.012). This dosage regimen was well tolerated. In conclusion monthly infusions of 90 mg. pamidronate in addition to hormone therapy are superior to hormone therapy alone in preventing SREs in stage IV breast cancer patients.

PP-8-9 Reduction of Skeletal Related Complications in Breast Cancer Patients with Osteolytic Bone Metastases Receiving Chemotherapy (CT), by Monthly Pamidronate Sodium (PAM) (AREDIA®) Infusion

G.N. Hortobagyi, L. Porter, D. Blayney, R.L. Theriault, A. Lipton, S. Gluck, H. Wheeler, S. Allan, J. Simeone, J. Seaman, R. Knight, M. Heffernan, D. Reitsma*. *Houston, TX; Brentwood, TN; Los Angeles, CA; Hershey, PA; Sudbury, ON; Sydney, Australia; Palmerston North, New Zealand; Boston, MA; Ciba, Summit, NJ*

We report the results of a randomized trial that compared the safety and efficacy of a 2-hour infusion of 90 mg of PAM q 3–4 weeks for 12 months (185 patients) to placebo (PL 197 pts) in preventing skeletal related episodes (SRE: pathologic fracture, cord compression, radiation or surgery to bone, hypercalcemia) in breast cancer patients with $\geq$ 1 osteolytic bone metastases of $\geq$ 1 cm in diameter treated with CT. At 12 months, the proportion of patients having any SRE was statistically significantly lower with PAM (43%) than with PL (56%, p = 0.008). The proportion of patients having any non-vertebral pathologic fracture or radiation to bone was less on PAM, than on PL, as was that of surgery to bone or spinal cord compression. The time to first SRE was longer in the PAM group (median = 13.1 m) than on PL (7.0 m, p = 0.005). Bone lesion response was assessed by X-ray at baseline, 6 and 12 m: CR + PR was 33% on PAM and 18% on PL (p = 0.001). At the last measurement, significantly fewer PAM patients (26%) than PL patients (36%) had an increase in analgesic score from baseline. Pamidronate was well tolerated. We concluded that monthly infusions of 90 mg pamidronate in addition to CT are superior to CT alone in preventing SRE's in Stage IV breast cancer patients.

POSTER PRESENTATIONS

PP-8-10 Breast Cancer in 1980–1995: Meta-Analysis of Dose Intensity (Neoadjuvant Chemotherapy)

J. Shparik. *Dept. Oncology, P.O. Box 2468, Lviv, 290029, Ukraine*

A positive relation between dose intensity (DI) and treatment outcome has been demonstrated not only in advanced breast cancer (BC) but also in adjuvant setting. Only few trials using DI concepts have been performed in neoadjuvant chemotherapy for BC. To determine if chemotherapy DI influences treatment outcome in BC, 41 published trials (some of which were not randomized) from 1984–1995 were retrospectively analyzed. Regimens included such agents as Cyclophosphamide (31 trials), Fluorouracil (26), Doxorubicin (24) or Epidoxorubicin (13), Methotrexate (9), Vincristine (6), Mitoxantrone (3), Cisplatin (2), Mitomycin C (1), and Tiotepa (1) (from single drug therapy to five-drugs combinations). Relative DI (RDI) of each study regimen was calculated against commonly used doses of each drugs in single regimens. Meta-analysis of chemotherapy trials for BC with some various regimens have suggested that higher total RDI correlated strongly with improved response rate (39 trials, r = 0.43, p = 0.0057) and slight but not significantly with complete response (29 trials, r = 0.36, p = 0.0539). It is first retrospective analysis on DI-response relationship in neoadjuvant chemotherapy of BC.

PP-8-11 Half Body (HBI) and Total Body (TBI) Irradiation in Disseminated Breast Cancer Patients (PTS)

V. Vinogradov*, L. Koritova. *Medical Academy for Postgraduated Studies, Central Research Institute of Radiology, St-Petersburg, Russia*

Between 03/1986 and 06/1993 HBI or TBI was performed in 33 breast cancer patients with bone, lung, liver, soft tissues or brain metastases. All pts but one had multiple lesions. The doses of 3 Gy (single-dose TBI), 5–6 Gy (single-dose HBI) or 19.8 Gy in 11 treatments (fractionated HBI) were delivered through opposite anterior-posterior fields, using 15 MeV linear accelerator. Boost accelerated irradiation was given on locally involved sites.