		Baseline	Week 8	p* (EXE vs MA)	p* (vs Baseline)
BAP	EXE (23)	24.9	30.1	NS	<0.01
(ng/mL)	MA (28)	23.8	24.2		NS
ICPT	EXE (23)	5.3	6.3	NS	<0.01
(ng/mL)	MA (28)	5.3	6.1		<0.05

p* Wilcoxon's test

effect, while the increase of both on EXE may suggest also the presence of an anabolic effect, possibly linked to the weak androgenic effect from the metabolite 17-hydro-exemestane.

708 POSTER

A phase II trial of zd0473 in patients with metastatic breast cancer. A National Cancer Institute of Canada clinical trials group study (NCIC CTG-IND 129)

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ZD0473 is a new generation platinum compound with significant activity against a wide range of cultured human tumour cell lines and against a panel of human ovarian xenografts, including cisplatin- and carboplatin-resistant cell lines. Phase I studies showed activity in several solid tumours including breast carcinoma, and at the recommended starting dose of 120 mg/m2 q 3 weeks (wks), the NCIC-CTG initiated a multicenter phase II study in metastatic breast cancer (MBC) in January 2000. Thirty-three patients (pts) have been enrolled. Thirty two pts are evaluable for toxicity and 25 for response at this time. Eligibility criteria included pts with no more than one prior chemotherapy for their MBC, performance status (ECOG 0-2), adequate organ function, measurable disease and informed consent. After the first11 pts experienced only minimal hematological toxicity, the starting dose was subsequently escalated to 150mg/m2 q 3 wks. Thirteen pts have received a total of 41 cycles at 120mg/m2, and 19 pts have received a total of 40 cycles at 150mg/m2. In the patients evaluable at this time, toxicity has been mainly hematological with grade 3 or 4 thrombocytopenia in 12/19 pts at 150mg/m2 and grade 3 thrombocytopenia in 3/13 pts at 120mg/m2. Grade 3 or 4 neutropenia occurred in 14 pts at the 150mg/m2 dose. At 120mg/m2, 2 pts had grade 3 or 4 neutropenia. Non-hematological toxicities have been generally mild to moderate and include nausea, vomiting, anorexia, fatigue, bleeding, taste disturbance, headache, constipation, alopecia and dyspnea. No complete responses have been seen but there has been one partial response and 13/25 pts have stable disease at this time. ZD0473 has modest activity as a single agent in MBC. Phase 1 combination studies with other agents including paclitaxel and docetaxel suggest increased activity which may be worthwhile in pursuing in the metastatic breast cancer setting.

709 POSTER

Gemcitabine, epirubicin and paclitaxel (GET) vs. 5-fluoro-uracil, epirubicin and cyclophosphamide (FEC) as first-line treatment in metastatic breast cancer: interim toxicity analysis of a randomised, multicenter phase iii trial of the Central European Cooperative Oncology Group (CECOG)

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Purpose: This phase III multicenter trial was initiated to compare the efficacy and toxicity of GET vs. FEC as first-line therapy in patients with metastatic breast cancer.

Patients and Methods: 84 female patients were enrolled into the study between October 1999 and March 2001. Out of those, 78 patients are available for analysis of toxicity. 33 patients were randomized to receive gemcitabine (1000 mg/m2, days 1+4), epirubicin (75 mg/m2, day 1) and paclitaxel (175 mg/m2, day 1), whereas 45 patients received 5-fluorouracil (500 mg/m2, day 1), epirubicin (75 mg/m2, day 1) and cyclophosphamide (500 mg/m2, day 1). Both regimens were administered in 21-day- courses up to a maximum number of 8 cycles. The median age of patients was 54 years (53 years in the GET and 55 years in the FEC arm) with a median of 6 administered cycles (range: 1-9) in both treatment arms.

Results: Myelotoxicity represented the major toxicity and included neutropenia of grades 3 & 4 occurring in 93.9% of patients receiving GET vs 73.3% of patients receiving FEC, thrombocytopenia of grades 3 & 4 in 27.3% vs 4.5% and anemia grades 3 & 4in 18.2% vs 11.4% of patients. Febrile neutropenia occurred in 3 patients treated with GET vs 2 patients receiving FEC. Peripheral neurotoxicity grades 1 & 2 were observed in 45.2% of patients in the GET arm vs 11.4% of patients in the FEC arm. No clinically apparent left ventricular dysfunction or failure were found in either group of patients.

Conclusion: While recruitment of patients is continuing, we conclude from this interim analysis that GET has a favourable and acceptable toxicity profile, as compared to the FEC regimen. These results warrant further clinical trials on the efficacy of the GET regimen.

710 POSTER

A phase II multicenter trial of weekly herceptin with navelbine in chemonaive patients with her2 positive metastatic breast cancer

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Background: Herceptin (H) is a well tolerated agent with documented efficacy in breast cancer and pre-clinical synergy with Navelbine (N). This combination has been found to be active in a single institution trial of largely pre-treated breast cancer patients (N at 25mg/m2/wk; Burstein et. al. ASCO 2000).

Purpose: We designed this phase II multicenter study to assess the efficacy and safety of H+N as first-line treatment for HER2 overexpressing metastatic breast cancer patients with measurable disease.

Patients and Methods: Eligible women were treated with weekly IV doses of H (4mg/kg loading dose, then 2mg/kg) and N (30mg/m2) without a break, with 4 weeks comprising a cycle.

Results: As of April 15, 2001, 37 of the planned 40 patients have been entered. Patient characteristics are: median age 51 years (range 30-82); prior adjuvant chemo 29%; prior hormonal therapy 32%; visceral metastases 58%. Twenty-nine patients are evaluable for response, having received at least 2 cycles. Two CRs and 19 PRs have been observed with an overall objective response rate of 72%, while 5 patients are stable and 3 progressed. Median time to response was 8 weeks. To date, a total of 188 cycles have been administered (median 4, range 1 to 26) with dose delays in 32% of the cycles Grade 4 toxicity was limited to neutropenia experienced by 25% of patients in 8% of cycles, while 51% of patients experienced Grade 3 neutropenia in 23% of cycles. Four patients were hospitalized with fever (1 neutropenic, 1 line sepsis, 1 with tuberculosis, 1 with pneumonia), 1 patient with hematura (due to over anti-coagulation from coumadin) and 1 patient with pulmonary embolism. Non-hematologic toxicity of fatigue was observed as grade 3 in one patient and grade 4 in another patient. No severe nausea, vomiting, cardiotoxicity, neurotoxicity, or alopecia has been reported.

Conclusion: These preliminary results suggest that H+N is well tolerated and very active in this patient population. Supported by grants from Genentech Inc. and GlaxoWellcome Inc.

711 POSTER

Dose-finding study of Docetaxel (T) and Doxorubicin (A) day 1 and 8 plus Capecitabine (X) day 1 to 14 (TAX) as first line treatment in advanced breast cancer (ABC)

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Background: Early results of T and Epirubicin (E) given on days 1 and 8 plus continuous infusion (c.i.) 5FU days 1 to 14 q 3wks (TEF) in 30 patients (pts) have shown that haematological toxicity was dose limiting (DLT) with G4 neutropenia and uncomplicated febrile neutropenia (FN) in 67% and 5% of cycles (cy) at the highest dose level (T40/E45/5FU200 mg/m2), respectively. Gastrointestinal (GI) toxicity seemed E-related (being the 5FU dose fixed at all dose levels) with ≥ G2 diarrhoea and mucositis in 6% and 18% of cy, respectively. In July 2000 a multicentric dose-finding study was launched to replace c.i. 5FU by X given days 1 to 14 with T and A on days 1 and 8 q 3wks (TAX).