No grade III/IV fluid retention or cardiac events were observed. Therapy was stopped preterm in 36 P (ADOC 17, AC-DOC 19) because of toxicity (17 P), progression (4 P), death (1 P), other causes (5 P), and for lack of compliance (9 P). In 26 of 193 (13.5%) P a pCR with no detectable viable tumor cells was confirmed.

Conclusion: Dose-dense combination or conventional sequence of adriamycin and docetaxel are feasible, well tolerated, and highly effective as preoperative CHT in primary operable breast cancer. The trial is planned to close in September 2001.

537 POSTER DISCUSSION

Preoperative trastuzumab (T) and paclitaxel (P) for HER2-overexpressing (HER2+) stage II/III breast cancer

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We conducted a phase II study of preoperative T&P, followed by definitive breast surgery and postoperative doxorubicin/cyclophosphamide (AC). The primary study endpoint was pathological complete response to preoperative therapy, defined as absence of invasive disease. Eligible women had HER2+ breast cancer (either +2 or +3 by IHC), clinical stage II or III disease, and LVEF > 50%. Preoperative treatments were T (4 mg/kg x 1, then 2 mg/kg weekly x 11) and P (175 mg/m2 every 3 weeks x 4 treatments). Adjuvant AC at standard doses of 60/600 mg/m2 respectively, every 3 weeks x 4, was begun after surgery and no less than 6 weeks after the final T dose. Cardiac function was assessed at baseline, following preoperative T&P, and after cycles 2 and 4 of AC. 40 patients (median age 49) were accrued to the study, having clinical stage II (55%) or III (43%) cancer (one patient had ipsilateral supraclavicular node involvement as sole site of metastatic disease). Initial biopsies were HER2 positive, 2+ (20%) or 3+ (80%). Asymptomatic grade 2 cardiac toxicity was seen in 4 patients, 1 following H&T, 3 during AC therapy. All 4 patients developed LVEF between 40 and 50%. One patient came off study following first T dose for hypersensitivity reaction. No other unexpected toxicity was observed. Pathological complete response was observed in 7 of 40 patients (18%). Objective clinical response (CR and/or PR) was observed in 27 of 40 patients (68%). Neoadjuvant T & P appears feasible in women with stage II/III HER2+ breast cancer, and has substantial clinical activity, particularly among women with HER2 3+ tumors. Cardiac function merits close surveillance in patients receive preoperative T & P followed by adjuvant AC.

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538 POSTER DISCUSSION

Efficacy and safety of three-weekly herceptin with paclitaxel in women with her2-positive metastatic breast cancer: preliminary results of a phase II trial

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Herceptin in combination with chemotherapy has been shown to increase survival in women with HER2 positive metastatic breast cancer (MBC). Herceptin has so far been administered weekly in most studies. A less frequent, 3-weekly treatment schedule would be more convenient for patients, doctors and treating institutions.

In this phase II study, patients received Herceptin at a dose of 8 mg/kg (loading) followed by 6 mg/kg every 3 weeks (maintenance) in combination with paclitaxel (175 mg/m2) every 3 weeks for 8 cycles. At this point, Herceptin was continued as monotherapy until progression of disease.

32 patients were recruited with a median age of 53 years (31-70). The majority (94%) of patients had metastatic disease: 50% lung metastases, 47% liver metastases and 19% a malignant pleural effusion at baseline. 81% of patients had 2 or more sites or organs involved. 68% had received previous treatment for MBC; 70% anthracyclines, 59% hormone therapy and 72% radiotherapy; 90% of patients were taxane naïve.

The median number of cycles (range) for paclitaxel was 6 (1-8) and for Herceptin 7 (1-22), counting 3 weekly doses as a cycle for Herceptin. 3 patients experienced infusion reactions during Herceptin infusion but were able to continue treatment. No serious cardiac events were reported: 5 patients experienced a decrease of more than 15% of their LVEF. The most common moderate to severe adverse events were (% of patients): myalgia (44%), arthralgia (31%), dyspnoea (16%), fatigue (6%), mucositis (6%), paresthesia (6%), headache (9%) and diarrhoea (9%). Grade 3 and 4 haematological toxicity was limited to neutropenia (grade 3, 13% of patients; grade 4, 3%).

Investigator assessed responses were: complete response 9.4%, partial response 43.8% and overall response rate 53% (95% CI 35-71); 25% of patients had stable disease. The median response duration was 6.3 months (1.5-13.4+) and 15 patients continue on treatment; the estimated median TTP is 10.9 months.

Preliminary data indicate that the efficacy and safety of this 3-weekly regimen of Herceptin with paclitaxel are similar to the standard, approved weekly regimen of Herceptin with paclitaxel (NEJM 2001;344;783-92). Further investigation of this 3-weekly Herceptin regimen is ongoing/planned in the metastatic setting (monotherapy) and it will be used in the HERA adjuvant study.

539 POSTER DISCUSSION

Cyclophosphamide (C) - Epirubicine (E) - Capecitabine (X) combination, CEX: A safe and active regimen in the treatment of locally advanced/inflammatory (LA/I) or large operable (LO) breast cancer (BC). An EORTC-IDBBC study

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Purpose: To evaluate the maximum tolerated dose (MTD) of X in combination with fixed doses of E (100 mg/m^2) and C (600 mg/m^2) q 3 weeks. To have preliminary information on the antitumor activity of the regimen by treating a cohort of 15 LA/I or LO BC patients (pts) at the MTD, for a maximum of 6 cycles.

Methods: Four dose-escalation levels (L) of X were planned: L1: 1500, L2: 1800, L3: 2100 and L4: 2400 mg/m^2/day from day 1 to day 14. Dose escalation was allowed if $\leq$1/3 or 1/6 pts experienced dose-limiting toxicity (DLT: febrile neutropenia: grade 4 neutropenia lasting $\geq$7 days; grade 4 thrombocytopenia; grade 3–4 non-hematological toxicity (NHT) other than alopecia; discontinuation of X for more than 8 doses due to toxicity). Eligible pts were $\geq$18 and $\leq$70 years old, had LA/I or LO BC and a WHO performance status (PS) 0–1.

Results: From February to December 2000, 23 pts entered the study (L1 = 3 pts; L2 = 3 pts; L3 = 15 pts: L4 = 2 pts). Major pts characteristics were: median age 48 years (range 33–68), PS 0 (23 pts): LA/1 BC (9 pts/9 pts); LO BC (5 pts). The MTD was identified at L3 since 2/2 pts treated at L4 experimented a DLT [grade 3 mucositis (1 pt) and grade 3 fatigue that led to X discontinuation for more than 8 doses (1 pt)].

Dose Level 3. *Drug administration* (15 pts/61 cycles): median number of cycles: 4. range 2–6; median relative dose intensity: 100%, 100%, and 96% for C, E, and X, respectively. *Safety data* (15 pts/60 cycles): G4 neutropenia (9 pts); febrile neutropenia (2 pts); no grade 4 NHT. Grade 3 NHT that occurred in >1 pts were nausea and palmar-plantar-crythrodysesthesia (2 pts each). *Activity data* (15/15 pts; WHO criteria): 1 CR; 10 PR; 4 NC. Median time to response was 44 days (range 30–83).

Conclusions: CEX is a safe regimen with a promising antitumor activity (RR 73%) in LA/1 and LO BC pts. Planned next step is to confirm the high activity of this association in a phase II trial.

540 POSTER DISCUSSION

A single, fixed-dose of Pegfilgrastim given once-per-chemotherapy cycle is as effecitve as daily Filgrastim in the management of neutropenia in high-risk breast cancer

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Purpose: Prophylactic use of Filgrastim (F) reduces the incidence and duration of chemotherapy-induced neutropenia (CIN), thereby decreasing the associated risk of infectious complications and compromised outcomes due to chemotherapy treatment delays and dose reductions. Pegfilgrastim (PegF) is a unique sustained-duration cytokine with self-regulating, neutrophil dependant pharmacokinetics. This randomized, double-blind,