Toxicity was assessed according to WHO criteria. Grade III–IV transitory neutropenia was identified in 29.8% and 19.4% of the courses administered respectively, only 5 pts received bone marrow rescue (G-CSF). Peripheral neuropaty grade I–II was seen in 36.6 pts and III–IV in two pts; one patient went out of study for neurotoxicity. No patient had evidence of cardiac toxicity. We achieved: 61.5% OR (20.5% CR, 41% PR), 25.7% SD and 12.8% PD; 75% of CR received (E) 90 mg/m^2 and (T) 200 mg/m^2. At the present time of the study the duration of response is as follows: CR median 10.4 months (6–18), PR median 8.7 months (6–13). Paclitaxel in combination with Epidoxorubicin represents an active and tolerable regimen for women with metastatic breast cancer. Further studies are warranted in order to modulate the neurotoxicity observed in our study by weekly administration of drugs.

42 POSTER

Timing of combined chemoradiotherapy in the conservative treatment of locally advanced breast cancer (LABC)

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The aim of this study was to compare the initial combination of chemotherapy and irradiation to a delayed association after neoadjuvant chemotherapy (CT) in a conservative treatment of LABC. From 1988 to 1993, 65 patients with stage III breast cancer were included in this randomised study. Median age was 49 years, 71% of the patients were premenopausal. In group 1, patients (N = 34) received a split course radiotherapy (RT) of 18 Gy during 2 weeks, on week, 1, 5 and 9 with concomitant CT (VCF) that consisted of vindesin (V) 3 mg/m2 day (d) 1 and 5, cyclophosphamide 300 mg/m2 d 1 and 5 intravenously and fluorouracil (FU) 600 mg/m2 continuous infusion from d 1 to 5, every 3 weeks. Boost RT of 18 Gy was delivered on tumour site at week 13. Three weeks after RT, patients received monthly (AVCF) Adriamycin (A) 25 mg/m2 d 1 and 2, C 400 mg/m2 d1, 2 and 3, V3.5 mg/m2 d 1 and FU 500 mg/m2 from d1 to 5 during 8 months. In group 2, patients (N = 31) received 3 monthly neoadjuvant AVCF, followed by RT of 54 Gy during 6 weeks associated with VCF, each 3 weeks. Three weeks after a boost RT of 18 Gy, 5 monthly AVCF were delivered. Total treatment duration was 12 months in both groups. Median follow-up time is 7 years. Objective response rates were 88% in group 1 and 77% in group 2. Mastectomy had to be performed after RT in 3 cases (9%) and in 7 (23%) respectively. Five years probabilities for survival without local recurrence were 74% and 78% in group 1 and 2 respectively (p = 0.38), 63% and 66% for survival without metastases (p = 0.56), 52% and 58% for disease-free survival (p = 0.24), 73% and 79% for overall survival (p = 0.77) and 72% and 60% for breast conservation (p = 0.67). In conclusion, combined chemoradiotherapy with prolonged adjuvant CT has efficacy in LABC, with a high 5-year survival rate of 76% and a breast conservation rate of 66%. We did not to find any difference between initial versus delayed radiotherapy in this study.

43 POSTER

Primary chemotherapy for locally advanced breast cancer using film as a novel regimen

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Sixty nine patients with locally advanced carcinoma of the breast were treated with Neo Adjuvant combination chemotherapy regimen between October 1993 and October 1997. The median age of the patients was fifty three (25–70). All patients received Neo Adjuvant chemotherapy consisting of 6 cycles of 5 FU, Ifosfomide, Leucovorin and Mesna at three weekly intervals. At alternate cycle Mitomycin C was added. Following chemotherapy 77% (53) underwent surgery [75.5% (40) received radiotherapy and 24.5% (13) did not receive radiotherapy] and 23% (16) patients did not undergo surgery [81.25% (13) received radiotherapy]. 46.4% (32) patients underwent mastectomy, 30.4% (21) underwent breast conservation surgery and 23.2% (16) had no surgery. The median disease free interval is 20 (6–51) months and the median survival period is 22 (7–53) months. The clinical response in these patients is 90% (23 CR, 39 PR). The pathological response in these patients is 85.5% (5 CR, 54 PR). The response rate and survival data are encouraging. Further trial are needed to confirm results.

44 POSTER

Letrozole as primary medical therapy for locally advanced and large operable breast cancer

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The aim of this study was to investigate the efficacy of letrozole given as primary systemic therapy and to compare responses with those obtained with tamoxifen. 24 patients were treated with letrozole (12 at 2.5 mg, 12 at 10 mg) and in a separate but identical protocol 65 patients were treated with tamoxifen. All were similar stages $T_2 > 3$ cm, T_3, T_{4b}, N_{0-1}, M_0. All tumours were ER +ve. Patients were monitored by monthly ultrasound and change in volume over a 3 month period calculated. The median percentage reduction in tumour volume with letrozole was 81, 95% CI 69–86. Prior to letrozole 15 patients would have required mastectomy but after 3 months therapy all were suitable for treatment by breast conservation. There was 1 complete pathological response and 3 patients had residual microscopic tumour foci only at the time of definitive surgery. In a series of 65 patients treated with tamoxifen, the median percentage reduction in tumour volume was 48, 95% CI 27–48. Although not a randomised study this was a much lower reduction than that obtained by letrozole. Letrozole is highly effective as primary systemic therapy and appears at least as good as tamoxifen in this setting.

45 POSTER

Weekly cisplatin-epirubicin-paclitaxel in advanced breast cancer: A phase I study

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Purpose: To determinate the MTDs of epirubicin (EPI) and paclitaxel (PTX) given weekly with a fixed dose of cisplatin (CDDP).

Methods: Breast cancer patients with advanced disease received CDDP at the dose of 30 mg/m2 togheter with escalating doses of PTX and EPI, weekly for a minimum of 6 cycles.

Results: To date 57 patients have been entered onto this phase I study, for a total of 410 weekly cycles delivered. Both hematological and non-hematological toxicity have been manageable. Overall 8 pts. have shown DLT (neutropenia causing a >2-week cumulative delay in 4 pts, peripheral neuropathy, cardiac ischemia, and severe diarrhoea in 1, 1, and 2 pts. respectively). Only 2 pts. have required hospitalization because of sepsis. Grade 4 thrombocytopenia has never occurred, but severe anemia has occurred quite frequently as the treatment went on, with 18 pts. requiring blood transfusions. Alopecia has been almost universal. Other nonhematologic toxicities have been generally mild except for grade 3 fatigue, vomiting and diarrhoea occurring in 4,7, and 3 cycles respectively. Peripheral neuropathy has occurred in 12 pts., but was severe in 1 case only. 12 complete and 35 partial responses have been registered for an 82% ORR.

Conclusions: The recommended doses of EPI and PTX to combine weekly with CDDP 30 mg/m2 are 40 mg/m2 and 85 mg/m2 respectively, in absence of G-CSF support. Although less than 33% of pts. enrolled at level 5 showed DLT during the firs 6 cycles, we stopped the escalation since the actually delivered dose intensity was less than 70% of that planned in more than 50% of pts. The escalation still continues with the concomitant administration of G-CSG (5 mg/kg d 3–5 of each week), and the PTX and EPI doses can be safelty escalated to 120 mg/m2 and 50 mg/m2/week in this way. This approach appears to be higly effective (82% ORR with 22% CRR) and deserves a further evaluation in large phase II/III trials either in advanced or inoperable breast cancer.

46 POSTER

Long duration of response with letrozole 2.5 mg (Femara®) in two trials in postmenopausal women with advanced breast cancer after anti-estrogen therapy

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Purpose: Subset analyses on duration of response and time to progression