We prospectively studied 36 women (age range 25 to 58) with breast cancer receiving single agent doxorubicin (75 mg/m^2) as part of their adjuvant therapy. They had normal baseline ECG, liver biochemistry and 2-D echocardiography. Blood was taken 30 minutes after the first bolus injection for metabolite analysis. Echocardiograms were repeated at 3 and 9 weeks, prior to further doxorubicin doses and at 1 year.

57% of patients had Dol 7-d levels, ranging from 2 to 90 ng/ml. No patient developed cardiac failure (mean drop in LVEF of 3.5% after 1 year). Significant differences in diastolic function (Peak E) were found by 9 weeks (paired t-test, $p < 0.01$) which persisted at 1 year (paired t-test, $p < 0.05$) but not linked with LVEF changes. Dol 7-d levels at 30 minutes correlate with Peak E changes at 9 weeks (Kendal's rank correlation coefficient, $p < 0.01$) but not at 1 year ($p < 0.1$) and not with other variables such as age or smoking history. These results support the hypothesis that Dol 7-d levels are associated with early free radical damage to the heart but not with long term cardiotoxicity.

798 POSTER

GEPARDO – A German trial of preop. chemotherapy with ADoc in breast cancer: First promising results

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Purpose: To assess the tolerability and efficacy of preoperative chemotherapy with adriamycin and docetaxel (ADoc) in patients with primary op. breast cancer.

Patients and Methods: In a prospective phase II-trial 195 patients with hi-stologically confirmed primary breast cancer (tumor > 3 cm, not T4) received dose-intensified adriamycin (50 mg/m^2) and docetaxel (75 mg/m^2) every 14 days and surgery after 4 cycles. Patients also were randomized to simultane-ous tamoxifen vs no tamoxifen. We report about an intermediate evaluation on 45 patients (T > 5 cm, N+ 58%)

Results: Response using best imaging was: CR 5%, PR 69%, NC 23%, PD 3%. Breast conserving surgery was performed in 74% of the patients. Hi-stol. CR was achieved in 6 patients (14.3%). Therapy was interrupted in 2 patients. Hemat. tox. III/IV 32/12%, gastroint.tox was mild as well as muco-sa and cutane tox..

Comclusion: 8 weeks of preop.Adocñtam efficiently reduce tumor size, achievehigh rate of PCR and breast concerving. Toxicity was well acceptable and tolerable in 95% of the patients.

799 POSTER

Endometrial changes caused by tamoxifen

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Purpose: Prolonged therapy with tamoxifen gives rise to endometrial abnormalities and has been reported to increase the subsequent development of endometrial cancer six fold. This prospective study was designed to examine the time course over which endometrial abnormlities occur in an adjuvant setting.

Methods: Patients requiring adjuvant tamoxifen as part of their normal treatment for breast cancer underwent baseline pelvic examination, transvaginal ultrasound scanning (TVUS) to measure endometrial thickness (ET) and biopsy for histology and insulin growth factor-1 levels if ET was >7 mm. Subsequent TVUS (and biopsy if ET > 7 mm) was performed at 1, 2, 3, 6, 12, 24 and 36 months.

Results: Twenty seven patients have been studied for a mean of 15.8 months. The mean endometrial thickness has increased from 3.45 mm before tamoxifen (0 months) to 4.99, 5.7, 5.3, 4.98, 4.85, 5.55 and 6.6 mm at 1, 2, 3, 6, 12, 24 and 36 months. After 6 months therapy with tamoxifen, 41% of women had an increase in endometrial thickness of >100% and this had risen to 50% of women after 12 months therapy but had decreased to 40% after 24 months therapy.

Conclusion: Tamoxifen causes a rapid initial rise in endometrial thickness, perhaps due to oedema, but then continues to increase endometrial thickness progressively with increased duration of use.

800 POSTER

Systemic therapy and acute reactions during adjuvant RT after conservative surgery in early breast cancer

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Purpose: To evaluate the influence of different adjuvant chemotherapy (CT) or hormone therapy (HT) regimens, on acute reactions during post-operative RT, in pts with stage I–II breast cancer treated in 12 Institutions of Northern Italy (Lombardy), in 1997.

Methods: The analysis concerns local toxicity (EORTC-RTOG scale) in 1610 pts (mean age 57 yrs, 69% post-menopausal, 31% N+). The whole breast was irradiated with 60Co or 4–6 MV photons at the mean ICRU dose of 50 Gy, plus a booster of 10 Gy in 1070 cases: 38% of pts had CT, 33.4% HT, 28.6% only RT.

Results: The incidence of acute skin reactions in pts treated with only RT was: grade (G)0 = 19.6%, G1 = 61.4%, G2 = 17%, G3 = 2%; in pts treated with HT: G0 = 14.3%, G1 = 66.2%, G2 = 17.3%, G3 = 2.2%; and in pts treated with CT: G0 = 12.4%, G1 = 62.2%, G2 = 21.1%, G3 = 4.3%. No acute toxicity involving lung or heart was detected. RT had to be interrupted in 35 cases owing to the toxicity of the combined treatment (RT + CT). There are no significant differences in acute cutaneous toxicity due to the types of chemotherapy (ADR based CT, CMF or others).

Conclusion: Post-operative RT was well tollerated, also with concomitant CT. The conclusive data including follow-up for cosmesis and survival will allow us to evaluate results and cost-effectivness according to different treatments and RT modalities.

801 POSTER

Concurrent sequencing of full dose CMF chemotherapy and radiation therapy in early breast cancer

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Purpose: The aim of this study was to evaluate whether the concurrent sequencing of CMF chemotherapy and adjuvant tangent breast irradiation effects the ability to deliver optimum doses of both treatment modalities.

Methods: Between the years 1986–1998, 105 patients were treated with CMF chemotherapy and radiation therapy. 67 were treated with concurrently (group 1) and 38 sequentially (group 2). Patients were well balanced with respect to age (48 vs 49 p = 0.9), no. positive nodes (0.3 vs 1), comorbid conditions (12.5% vs 10%) and breast seperation (18 vs 19.2). Mean follow up was 2.8 yrs. in group 1 and 3 yrs. in group 2.

Results: There was no significant difference in the % of prescribed chemotherapy actually delivered in the two groups (95% vs 95%), chemotherapy delay (7.4 days vs 6.6 p = 0.22), or nadir platelet and granulocyte counts (179 vs 187 p = 0.09, 1272 vs 1473 p = 0.06). There was a small but significant delay in radiotherapy delivery (1.85 days vs 0.4 p = 0.006). Of the patients followed for >2 yrs. 66%, 27% and 5% had excellent, good or satisfactory cosmesis in group 1 compared with 75%, 25% and 0% in group 2. There has been no local failures in group 1 compared with one (2.4%) in group 2 and 1 (1.4%) distant failure in group 1 compared with 4 (11%) in group 2 to date.

Conclusion: It is possible to safely deliver optimum doses of CMF chemotherapy and radiation therapy concurrently.

802 POSTER

Her 2 and topoisomerase (TOPO)IIα as predictive markers for node-positive (N+) breast cancer (BC) patients (PTS) randomised to adjuvant CMF or epirubicin (E) – cyclophosphamide (C)

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At ASCO '99 we reported the results of a clinical study where 777 pre- and post-menopausal N+ BC pts were randomised to: a) CMF (oral C) × 6; b) EC (E 60 mg/m^2, C 500 mg/m^2) d 1 i.v. q 3 wks × 8; c) high dose EC (HEC) (E 100 mg/m^2, C 830 mg/m^2) d1 i.v. q 3 wks × 8. The median follow-up is 50