frequent. Quality of life was significantly better according to the modified Brunner-Score in N compared to the FEC group.

Conclusion: As to the preliminary results the mono-compared to the poly-chemotherapy regimen didn't appear to show a difference in efficacy but a significantly better tolerability.

The study is on going.

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647 ORAL

Prospective randomized study of mitoxantrone (M) and vinorelbine (V) vs fluorouracil (F), epirubicin (E) or adriamycin (A) and cyclophosphamide (C) in patients with advanced breast cancer (ABC)

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Background: A woman with ABC has a life expectancy of 18–24 months under treatment and the key point thus remains quality of life. Side-effects most feared by women are alopecia, nausea/vomiting.

Methods: This study compared the new combination MV (M 12 mg/m^2 D1, V 25 mg/m^2 D1 and 8 if PN > 1000/mm^3) to FAC or FEC: F 500 mg^2, A or E 50 mg^2, C500 mg/m^2, D1. Stratification was based upon prior adjuvant chemotherapy (CT). Each cycle was repeated every 21 days.

Results: 281 patients (pts) were randomized between UV MV (142) and FAC/FEC (139). 89 pts had received prior adjuvant CT (76 with anthracyclins). 82% pts had visceral metastasis and the median number of metastatic sites was 2 (1–7). Overall, 698 MV and 841 FAC/FEC cycles were given (median/pt: 5 [MV]; 6 [FAC/FEC]). The mean dose intensity (%) was respectively 95, 96, 96 for FAC/FEC and 92, 77 for MV. Hematological toxicity delayed courses in 22% (MV) and 14% (FAC/FEC) and led to withholding of V on day 8 in 29%. Febrile neutropenia requiring antibiotics occurred in 6% (MV) and 0.6% (FAC/FEC) of cycles and led to hospitalization in respectively 16% and 3% of pts (p = 0.001). Cardiac events were mostly minor: 10 in FAC/FEC and 9 in MV. Grade 3–4 nausea/vomiting occurred in 8% [MV] and 16% [FAC/FEC] of pts (p = 0.03); alopecia was more frequent with FAC/FEC (p = 0.0001). Toxicity led to one death in each group. The objective response rates (OR) were similar: 35.5% [MV], 33.3% [FAC/FEC], p equivalency = 0.014) but the OR was higher in the pts on MV with prior adjuvant CT (33% vs 13%) and in those on FAC/FEC who had not (43% vs 35%). Time to progression and overall survival were not different in the two groups but showed a similar divergence when prior adjuvant CT was taken into account.

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648 ORAL

CAF vs CMF both with tamoxifen in postmenopausal patients with advanced breast cancer – A randomized study with more than 10 years follow-up from the Danish breast cancer cooperative group

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In the largest study ever reported comparing CMF-like regimens with CAF, postmenopausal advanced breast cancer (ABC) patients naive to chemotherapy <66 years accrued during 1980–84 and followed through 1995 received Tamoxifen daily 30 mg and cyclophosphamide 400 mg/m^2, doxorubicin 25 mg/m^2 and 5-fluorouracil 500 mg/m$_2$ (CAF) or methotrexate 40 mg/m^2 instead of A (CMF) i.v. days 1 and 8 q 4 weeks. A was substituted by M at a cumulative dose of 550 mg/m^2. Among 341 eligible patients (CAF 161, CMF 180) response rate and median time to progression was significantly in favour of CAF: 53% *vs* 36% (p = 0 002) and 11.8 months *vs* 6.5 months (p = 0.001). Duration of response was 19.5 *vs* 18.0 months, and survival 20.8 *vs* 17.4 months (ns). Treatment intensity and toxicity was equal. After 3 years 44 *vs* 38 patients were still alive. Long recurrence free interval, good status of performance, and no visceral involvement was significantly related to long survival, while treatment was not. At end of follow-up, 3 and 4 patients were still alive. Doxorubicin-containing regimens remain the first choice of chemotherapy for ABC until newer treatments have proved superior.

649 ORAL

Navelbine (NVB), and fractionated dose doxorubicin (DX) improves first line advanced breast cancer (ABC) chemotherapy. An overview of 3 phase II trials

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Aim: Anthracycline combinations represent the most powerful chemotherapeutic approach in the treatment of ABC, but their limiting toxicities are neutropenia and cardiac impairment. NVB as a single agent has demonstrated a high activity and good tolerance in ABC: 40%–60% response rate (RR). Promising results have previously been obtained with NVB 25 mg/m^2 D1 & 8 + DX 50 mg/m^2 D1 (q 3 w): 74% RR (21% CRs), mainly in visceral sites (JCO 94). This was confirmed by a significant survival advantage observed in pts with liver metastases treated with NVB + DX compared to CAF (ESMO 96). Dividing the DX dose and administering it at weekly intervals may reduce the cardiotoxicity without substantially impairing the efficacy. 3 studies were conducted with NVB + DX, both at 25 mg/m^2 D1 & 8 (q 3 w, 8 cycles) to check the efficacy, improve the tolerance and to ease outpatient administration.

Results: 120 pts were included: age 30–73y; PS 0–1: 85%; visceral involvement: 52%; adjuvant C: 18%. 668 18%.668 cycles were administered; WHO grade (G) 3–4 neutropenia: 24%; infection G 3: 6/120 pts; G 3–4 nausea/vomiting: 17 pts; G 3–4 constipation 1.5%; G 1 peripheral neuropathy: 13%; G 3 alopecia: 53.5%. No G 3–4 cardiotoxicity. The RR ranges from 70% to 77% (18–35% CRs) RR on visceral sites: 56%–86%.

Conclusion: These results confirmed that NVB + DX (25 mg/m^2 D 1 & 8) has major and reliable activity as 1st line therapy. Given its very favourable tolerance, low morbidity and absence of life threatening cardiotoxicity, out patient administration of this regimen could be recommended as 1st line treatment for ABC.

650 ORAL

Taxotere™ (docetaxel, D), doxorubicin (Dx) and cyclophosphamide (CTX) (TAC) in the treatment of metastatic breast cancer (MBC)

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Considering the promising results of combination of taxanes and anthracyclines, we conducted a phase II study of D (75 mg/m^2, 1 hour iv infusion) with Dx (60 mg/m^2, iv bolus) and CTX (500 mg/m^2, slow iv bolus) q.3 weeks (maximum 8 courses) in patients (pts) with MBC without prior anthracyclines or taxanes. Forty-five pts (238 courses delivered) were treated as follows. Characteristics: moan age: 52 years (34–70); prior adjuvant chemotherapy (CMF) 10 pts (22%); visceral metastases 29 pts (64%); bone 24 pts (53%); 3 and more sites: 18 pts (40%). Median follow-up: 7 months (3–11). Thirty-three pts are evaluable for response. The major response rate is 85% with CR: 4 pts (12%), PR 24 pts (73%), SD 5 pts (15%), PD 0 (0%), with no progression yet reported. Forty-five pts are evaluable for toxicity. Neutropenia is the main toxicity (grade 4: 78%, lasting less than 7 days), febrile neutropenia: 12.1% of courses (courses given with ciproflexacine (C): 10.8% and without C: 24%). There was no extrahematologic grade 4 toxicity, while Grade 3 occurred in 25 cycles (10.5%) (nausea/vomiting, pain, fatigue, diarrhea). Grade 3 fluid retention was seen in 1 pt (2.2%). No clinical cardiotoxicity occurred while 5 pts presented with a moderate asymptomatic and usually reversible decrease of LVEF on MUGA scan (11.1%). TAC is a well-tolerated and active regimen with no evidence of cardiac toxicity and is the base of 2 large international randomized multicentric randomized trials comparing TAC to FAC in metastatic and adjuvant setting.

651 POSTER*

Treatment of recurrent cutaneous metastatic breast cancer with tin ethyl etiopurpurin (SnET2) photodynamic therapy

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Introduction: Breast cancer recurrence of the chest wall following mastectomy, radiation and chemotherapy poses a therapeutic dilemma. Further intervention with any or all of these modalities is often futile and morbid. Left untreated severe pain, infection and suffering will occur. Photodynamic therapy presents as a palliative option for these individuals.

Materials and Method: A total of 42 lesions were treated on 5 patients of who had biopsy proven chest wall recurrence despite mastectomy, chemotherapy and radiation. Each patient underwent a single photodynamic therapy session in which the drug SnET2 (1.5 mg/kg) was injected followed 24 hrs later by laser by laser light treatment at 665 nm (@150 m W/sq.cm. for a total light dose of 200 J/sq.cm).

Results: Objective response rates post PDT were CR 92% PR 8% NR 0% Morbidity was minimal with no systematic toxicity. One patient developed a wound infection that responded to oral antibiotics. No photosensitivity reactions were reported in this set of patients. Post treatment pain was reported in patients, which could be treated with medication and application of cod compresses.

Conclusions: PDT offers an excellent local control rate of chest wall recurrence following multimodality treatment failure with minimal morbidity. The treatment is given in a single session and on an outpatient bases. In patients who may register a PR or have recurrence or the incidence of further chest wall nodules post PDT, the treatment is repeatable. No resistance or enhanced morbidity is demonstrated to a second or third course of PDT.

652 POSTER*

Response to primary chemotherapy of breast cancer

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The aim of this study was to evaluate mammography, ultrasound and dynamic MRI for response monitoring in primary chemotherapy of breast cancer.

Patients and Methods: 200 women with breast cancer have been treated by primary chemotherapy after core biopsy. Response was monitored before each chemotherapy cycle and before operation by mammography and ultrasound. 25 women have been monitored using a specially designed dynamic TurboFLASH MRI-technique with a high temporal resolution.

Results: Following chemotherapy the correlation of imaging with histopathological size was reduced. In diffusely spreading tumors histopathological tumor size was usually larger than estimated. Unchanged microcalcifiations of the ductal type still reflected the extension of the tumor. Altered tissue distribution of gadolinium in dynamic MRI after 2 cycles of chemotherapy correlated with histopathological tumor regression. By WHO criteria 10% of T_{2-3} tumors showed complete regression on imaging, 55% showed partial remission, 32% showed no change, 3% progressed. Pathohistologically 6% showed no invasive tumor, 18% showed invasive tumor below 5 mm, a further 27% showed clear signs of regression.

Conclusion: Mammography, ultrasound and MR can be used to monitor the response of breast carcinomas under primary chemotherapy. Dynamic MR shows promise for early prediction of tumor response. All three methods have limitations in the determination of preoperative extension of residual tumor.

653 POSTER*

Response to chemotherapy is the first prognostic factor in metastatic breast cancer

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Purpose: In a retrospective analysis of a large series of patients (pts) with metastatic breast cancer treated by chemotherapy (CT), prognostic factors for survival were evaluated.

Methods: 1430 pts included from 1977 to 1992 in eight consecutive randomized trials of anthracycline-based first line CT in metastatic breast cancer, were analyzed. Response to CT was assessed after 4 and 8 months of treatment.

Results: Objective response rate was 60%, 228 (16%) pts achieved complete responses (CR). Median overall survival (OS) was 24 months. At multivariate analysis for prolonged survival, response to CT was the first prognostic factor followed by normal LDH level, absence of previous adjuvant chemotherapy, 2 or less metastatic sites, longer disease-free interval from initial diagnosis, high Karnofski index and absence of hepatic metastasis. For pts with CR, partial response, stable disease and progressive disease, median OS and probability of survival at 5 and 10 years were respectively: 45 mths, 34%, 12%; 31 mths, 21%, 7%; 23 mths, 12%, 3%; 9 mths, 3%, 0%. Date of the first observation of CR, at 4 or 8 mths of CT, was not a predictive factor of duration of OS.

Conclusion: Response to an anthracycline-based chemotherapy is the first prognostic factor in metastatic breast cancer and is independent of the other disease characteristics. Prolonged survival can be achieved in pts with CR justifying research for remission consolidation strategies.

654 POSTER*

Dose finding study of high-dose epirubicin (E) and docetaxel (T) as first line chemotherapy in advanced breast cancer (ABC)

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Purpose: Primary objective of the present study is to determine the maximum-tolerated doses (MTDs) of E and T, given q 3 weeks, in pts with ABC without a prior chemotherapy (C) for metastatic disease and no anthracycline-containing adjuvant C. MTDs with G-CSF support were then to be defined.

Methods: E (15 min inf.) followed after 1 h by T (1 h inf.) were given for a maximum of 4 cycles (cy) to prevent cumulative cardiotoxicity; T alone was continued for a maximum of 4 cy in responders. Steroids were given before and after T for a total of 3 days. CBC was performed twice a week, LVEF and tumour response were assessed every 2 cy.

Results: From 7/96 to 2/97, 19 pts received 57 cy of the combination at three dose levels. Starting doses were 75 mg/m^2 of E and 75 mg/m^2 of T. E doses were increased to 90 mg/m^2 and 120 mg/m^2, while the T dose was kept at 75 mg/m^2. Haematological toxicity (HT) is evaluable in 15 pts. grade 4 neutropenia was universal, lasting a median of 4 days. Median neutrophil nadir was 0.23 $\times$ 10^9/l, significant thrombocytopenia or anemia were absent. At E 90 mg/m^2 and T 75 mg/m^2 3/6 pts required G-CSF support (neutropenic fever: 2 pts, grade 4 neutropenia of >7 days: 1 pt). G-CSF was routinely given at the dose level of E 120 mg/m^2 and T 75 mg/m^2. Non HT was mild; neither moderate to severe mucositis nor cardiotoxicity were observed. Partial responses were achieved in 11/13 pts.

Conclusions: The next dose level will be E 120 mg/m^2 and T 85 mg/m^2 with G-CSF support.

655 POSTER*

Toxicity and effect of single agent vinorelbine (V) in anthracycline-resistant metastatic breast cancer (ARMBC). Preliminary results of a phase I–II study by the danish breast cancer cooperative group (DBCG)

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ARMBC is a disease entity with a dismal prognosis. Recently, a number of drugs have demonstrated activity of which V is of particular interest because of its relatively low toxicity. The aims of the present study were to define the maximum tolerated dose (MTD) of V when administered on days 1 and 8 q 3 w and assess associated toxicities. From 11/95 to 10/96 54 patients with measurable or evaluable ARMBC and PS $\leq$ 2 entered the phase I part of the study. Dose of V was escalated from 25 mg/m^2 by 5 mg in cohorts of 8 patients until grade IV haematological or grade III non haematological toxicity (WHO) was recorded pre-cycle 2 in $\geq$50% of the patients. If additional patients were registered for treatment at a given dose level before toxicity pre-cycle 2 could be evaluated the patient was allocated to treatment at the lower dose level. The MTD has been reached at 40 mg/m^2. Median WBC nadir 1.0 (0.7–6.7) $\times$ 10^9/1. Dose limiting toxicities included grade III constipation and oral stomatitis in 5/8 evaluable patients. Other common toxicities have been nausea, vomiting, diarrhoea, infection, fever, local phlebitis, none of which have been dose limiting. At the first evaluation (pre-cycle 4) complete and partial responses have been recorded as follows: 25 mg 2/7, 30 mg 4/13, 35 mg 2/7. The phase II part of the study is ongoing at 35 mg/m^2.