applications with 20–160 W over 75 min. In group 2, median epicutaneous temp. of 41.2°C (40.0–42.0°C) and max. temp. 41.9–44.0°C were recorded in a median 10 (3–23) applications with 10–45 W over 60 min. In group 1 2/6 pat. presented with blisters/necrosis whereas no blisters were seen in group 2. Moist desquamation occurred in 2/6 pat. and 3/11 pat. in group 1 and 2, respectively.

Conclusion: To avoid hyperthermia induced blisters/necrosis epicutaneous temp. mapping is most important. In case of lymphangiosis cutis or infiltrated skin, bolus temp. of 40°C provide homogeneous heating of the chest wall. Large applicators increases the risk of "hot spots" and blisters/necrosis.

688 PUBLICATION

Taxol (T) and mitoxantrone (M) as first line treatment in advanced breast cancer (ABC) patients. A phase II study of the Southern Italy oncology group (GOIM)

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Purpose: In phase I/II studies the combination of T with anthracyclines yielded response rate ranging from 63% to 94%, sometimes with significative cardiotoxicity. In prospective randomized trials, M has shown a clinical activity only slightly inferior to that of anthracyclines, but with less incidence of alopecia, nausea/vomiting and cardiotoxicity. In view of these considerations, in April 1996 we started a phase II study with the combination of T and M as first line treatment of ABC.

Methods: Patients with histologically proven diagnosis of ABC, age between 18 and 65 years, adequate haematologic and normal renal, hepatic and cardiac functions, were elegible for the study. T was administered as a 3-hour intravenous infusion after standard premedication with steroid, antihistamine and H_2-blockers at a dosage of 175 mg/m^2; M was administered intravenously at a dosage of 12 mg/m^2. Courses were repeated every 3 weeks.

Results: To date, 23 patients were enrolled in the study and 16 are fully evaluable for clinical efficacy and toxicity. We obtained 4 CR, 7 PR and 5 SD for a total of 11 OR (69%) with a median duration of response of 6+ months and a median duration of survival of 7+ months. Toxicity was mild and mainly of grade I–II according to WHO criteria.

Conclusion: From our preliminary data of this ongoing study, the combination of T and M seems to be an effective and safe chemotherapy regimen for patients with ABC.

689 PUBLICATION

Factors predicting response to chemo-endocrine treatment in advanced breast cancer

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Purpose: Chemo-endocrine treatment as used in our institution is well tolerated even by heavily pretreated patients with advanced breast cancer. In a retrospective study the response rate and duration of response to this treatment regime was evaluated to find factors that predict good response to this treatment.

Methods: Response (CR, PR, NC) of 129 patients with metastatic breast cancer to chemo-endocrine treatment using Cyclophosphamide (100 mg/d p.o.), Methotrexate (25 mg/week i.v.), 5-Fluorouracil (500 mg/w i.v.), Prednisone (10 mg/d p.o.) and Methenolone (300 mg/w i.m.) was evaluated in correlation to steroid receptor status, prior disease-free interval, site of metastatic disease and previous treatement.

Results: Response rates were higher in patients with estrogen-and/or progesterone receptor positive tumors (80% vs. 37% in hormone-receptor negative), with long disease-free interval (78% in patients >2 years vs. 66% in patients <2 years), and with endocrine pretreatment (85% vs. 35% with chemotherapeutic pretreatment). Patients with bone metastasis showed better response (77%) than women with other metastatic sites (61%). Response rates were 73% with two and 68% with three previous treatment regimes.

Conclusions: Combined chemo-endocrine treatment is most effective in patients bone metastasis, positive receptor status and after response to prior endocrine therapy and is showing good response rates even in pretreated patients.

690 PUBLICATION

Phase II study of i.v navelbine (NVB) and doxorubicin (DOX) in previously untreated advanced breast cancer (ABC)

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Promising results have previously been obtained with the combination of NVB and DOX. 74% of the 89 patients (pts) responded with 21% CRs (JCO, 1994 Spielmann). A phase II study was conducted in South Africa in order to confirm these results with I.V NVB 25 mg/m^2 D1 & D8 + DOX 50 mg/m^2 IV on D1, every 21 days, for 8 cycles maximum. Forty chemotherapy-naive pts with ABC were treated. Up to now, 24 pts are evaluable for tolerance and response. Median (m) age was 47.7 y (25–69). All pts had Good PS: 0–1. At the inclusion, 77% pts had metastatic disease and 70% had extensive loco regional disease (m. size of local disease = 80 mm Ø, (range 20–140). 60% pts had ≥3 metastatic sites of which 45% were visceral (38% liver and 7% lung). In total, 223 cycles were administered (m per pts: 5, range 1–8). The overall response rate was 54% (CR 8%, PR 46%/95 CI 34–74%). 2 further pts obtained an objective response but were not available for confirmation. Pt's WHO grade 3 toxicity was as follows: Alopecia 69%, nausea/vomiting 15%, stomatitis 11.5%, phlebitis 4%. WHO grade 3 neutropenia was observed in 27% pts and grade 4 in 15% pts (2 of whom died). Grade 1 peripheral neuropathy was only observed in 4 pts (15%). No cardiac impairment was observed. Given the large tumor bulk of local disease in these patients, very good results and tolerance were documented.

691 PUBLICATION

The LHRH analogue triptoreline (TRP) with or without the aromatase inhibitor formestane (4-OHA) in premenopausal advanced breast cancer: A study by the I.T.M.O. group

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Purpose: This pilot study was undertaken by our group with the aim of acquiring information on the feasibility and toxicity of combined TRP and 4-OHA treatment in premenopausal patients (pts) with previously untreated advanced breast cancer.

Methods: 28 consecutive pts were randomised; 15 pts received TRP 3.75 mg i.m. monthly alone, and 13 pts received it in combination with 4-OHA 500 mg i.m. fortnightly. Eligible pts had to have measurable lesions, ECOG PS 0–2, and ER and/or PgR positive tumours. Postmenopausal status was defined as last menstrual period more than 1 year ago. Blood samples for measuring serum oestrogen and gonadotrophin levels were taken before and during treatment.

Results: There was no difference in terms of age, DFI, and PS between the two groups; 32% of pts had multiple disease sites. The intent-to-treat analysis showed objective responses in 27% of pts (2 CR + 2 PR) on TRP and in 31% (1 CR + 3 PR) on TRP + 4-OHA. The median duration of response in the two groups was 16+ months (range, 7+–21) and 11+ (range, 7–16), respectively. The sites of response were soft tissue (3 CR) and viscera (5 PR); SD occurred in 5 pts on TRP, and in 4 on TRP + 4-OHA. Local and systemic tolerability was highly satisfactory in both treatment groups. The endocrine evaluations are in progress.

Conclusion: In our experience, the concurrent use of TRP and 4-OHA proved to be a feasible and well tolerated approach in the management of premenopausal advanced breast cancer.

692 PUBLICATION

Are new anthracycline dose recommendations needed for patients with liver dysfunction?

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Purpose: To investigate whether U.K. oncologist follow current anthracycline dose modifications when treating patients with liver dysfunction.

Methods: One hundred and seventy oncologists replied to a questionnaire asking the % of full dose doxorubicin or epirubicin they would prescribe

a woman with breast cancer and liver metastases (but no bone metastases) who had one of 4 different patterns of abnormal liver chemistry.

Results:

Liver tests (normal)			% dose	Mean % dose	Preferred drug
Bili (<18)	AST (<35)	ALP (<260)	recommended	given (range)	dox/epi/either (%)
16	87	186	100	94 (0–100)	40/32/28
12	166	739	100	85 (0–100)	39/33/28
30	132	190	50	67 (0–100)	41/36/23
54	115	169	25	50 (0–100)	40/40/20

Conclusions: Dose modifications varied widely and did not follow current recommendations. There was a trend for epirubicin to be preferred for patients with the worst liver biochemistry. These results show the need for new, widely accepted anthracycline dose modifications for patients with liver dysfunction.

693 PUBLICATION

High dose sequential (HDS) cyclophosphamide (C) and epirubicin (E) with peripheral blood stem cell (PBSC) for metastatic breast cancer (MBC): Promising results

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Survival in MBC remains poor with conventional chemotherapy (CC) and does not appear to be substantially improved with late high-dose chemotherapy with stem cell support. HDS induction chemotherapy appears more promising. We report the preliminary results of a phase II study with HDS C + E in MBC. C (1500 mg/m^2 d1&2 with uromitexan) and E (100 mg/m^2 d1) were given every 2 wks × 4, with G-CSF 5 μg/kg/d × 10. PBSC were harvested after cycle 1, and reinfused after cycle 3&4. After HDS C + E, pts received 6-months of CC. 26 pts are evaluable (median age: 39 y). 9 pts (35%) had prior adjuvant chemotherapy (4 with anthracyclins) Visceral involvement was present in 16 pts (61%). The median number of collected CD34 + was 14.10^6/kg (3–81). Median relative dose intensity was 93% (72–100). No toxic death was observed. 1 pt received only 3 courses because of hematuric cystitis. Median durations of gr 4 neutropenia were 4, 5, 8 and 5 d for each cycle. Febrile neutropenia was observed after 36/101 courses (36%). Only 9 pts experienced a gr 4 thrombocytopenia. A mean of 6 RBC units/pt were transfused. Other toxicities were: gr 2–3 emesis 42%, gr 2–3 mucositis 21%, gr 2–3 liver toxicity 12.5%, and gr 3 alopecia 100%. Results in 25 evaluable pts were: CR 3, PR 14, for a RR of 68% (1 TE). After a median follow-up of 14 m, 2-y-overall survival was 85% and 1-y-progression free survival (PFS) was 74%. Median PFS was 21 months. This regimen is feasible and yields very encouraging survival rates despite conventional response rates.

694 PUBLICATION

Weekly fractionated paclitaxel in metastatic breast cancer – Dose optimising study

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Purpose: A recently published weekly fractionated, dose-intensified schedule of paclitaxel at 90 mg/m^2 weekly × 6, q9w, showed high efficiency and low toxicity Furthermore, patients seemed to have improved their quality of life (QOL).

Methods: As primary endpoints, we analyse the objective response rate. As secondary end points we focus on toxicity according to the WHO classification and on quality of life which is evaluated by a standardised psycho-oncological questionnaire. Neurotoxicity is monitored by electrophysiologic examinations.

Results: Up to now, 23 patients have been included in the study, 14 of whom are already evaluable for response. 4 pts had a partial remission giving 29% of response. In a total of 215 weekly infusions, we observed no anaemia WHO grade III and no cases of thrombocytopenia <100 000 cells/μl. Leucopenia WHO grade III was observed in 1% of all infusions The evaluation of the nerve conduction velocity did not help to foresee or assess neurotoxicity All patients suffered from grade III alopecia. According to the statistical analysis the quality of life is not improved. The median QOL score decreased from 3.79 before treatment to 3.55 after two cycles, but this difference was not statistically significant (p = 0.099).

Conclusions: In metastatic breast cancer weekly fractionated paclitaxel shows a high response rate of 29%. Hematological toxicity is insignificant. Among the non-hematological toxicities neuropathy is predominant. However, electrophysiologic parameters do not help in evaluating neurotoxicity. Although many pts show a regression of their tumor load, quality of life does not improve.

695 PUBLICATION

Brain metastases (BM) in breast cancer (BC): Prognostic factors and management in 162 patients

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Introduction: BC is one of the major causes of BM with about 10–15% of patients (pts.) developing clinically overt brain metastases. Prognostic factors for occurrence and outcome of BM in BC have not been identified.

Methods: In a retrospective study, we analyzed 162 BC pts., in whom BM had been diagnosed clinically between 1969 and 1996.

Results: The median age was 50 years (range 30–78). 81/162 pts. (50%) were premenopausal Women <40 years of age had a shorter survival (median 12 weeks) than those of all other groups (median 29 weeks). Median survival was 82 weeks for surgical pts. (n = 11), 26 weeks for pts. treated with radiotherapy (RT, n = 145) and 5 weeks for pts. who received symptomatic therapy only (n = 17). Pts. with solitary BM, treated with RT alone (45 pts.) had a survival of 44 weeks vs. 19 weeks in pts. with multiple BM Significant prognostic factors for survival were total dosage of RT (p < 0.0001), solitary BM (p < 0.04), and primary tumor size (p < 0.04). 5 pts. with solitary BM, no systemic disease and low grade BC, treated by surgery and RT, survived a median of 508 wks (range 262–520).

Conclusions: Younger pts. with aggressive histologies, especially inflammatory breast cancer, seem to have a higher risk for developing BM. Pts. with solitary BM should receive surgery and RT with a chance of long term remission.

696 PUBLICATION

Treatment and prognosis of male breast cancer: The Heidelberg experience

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As a rare entity Male Breast Cancer (MBC) represents 1% of all male tumors. Because of the reported worse outcome compared to female breast cancer (FBC), prognostic factors and treatment of MBC have to be evaluated.

Methods: 16 patients (Pt) treated at Heidelberg University from 1984–1997 were analyzed retrospectively. Median age at diagnosis was 55 (44–75) years. 14/16 Pt had an invasive ductal carcinoma; 9/11 Pt (82%) were progesterone and 7/11 Pt (64%) estrogene receptor +. 4 Pt were T1, 7 T2, 1 T3, 2 T4, 2 Tx; modified radical mastectomy was the initial therapy in all Pt. 9/15 Pt with axillary lymphonodectomy were N+. 1 Pt presented bilateral MBC.

Results: None of the Pt had a positive cancer family history. As in FBC, node-negative Pt had a better prognosis than Pt with lymph node involvement. However, the PR + status appeared to be related to a worse prognosis. After adjuvant CMF-chemotherapy (CT), 6×, and radiation of the chest or tamoxifen, 8 Pt (>T2N1) developed visceral metastases within 2 years, i.e. 50%; 7 Pt. (44%) developed bone metastases. In the palliative situation 5 Pt received EC-CT with 2 PR and 1 NC. 3 Pt treated with NOSTE-CT had 1 PR. Additionally, tamoxifen or aromatase inhibitors were used, palliatively. Median 3/5 year survival was 56%/47%, respectively.

Conclusion: Tumor size and nodal status were the most important prognostic factors. In the palliative situation Pt have a benefit from the EC-CT. The survival rates of MBC are comparable to FBC. The prognostic significance of the hormonal status and other molecular markers have to be further evaluated.