Patients and Methods: In total, 150 patients with HER2-overexpressing MBC (IHC 3+ [DAKO HercepTest] or IHC2+/FISH+) will be enrolled from approximately 30 centres throughout Germany. Patients previously treated with adjuvant chemotherapy and/or a single course of therapy for MBC are eligible for enrolment. Patients will receive two 6-week courses of paclitaxel (90mg/m^2/week i.v.), separated by a 2-week break. Concurrently they will receive weekly trastuzumab (4mg/kg i.v. loading dose followed by 2mg/kg/week i.v.); trastuzumab will be given for at least 48 weeks, or until disease progression.

Results: Currently 76 patients have been enrolled; data on 58 patients is discussed here. 89% had tumours with IHC 3+ overexpression, 11% had IHC2+/FISH+ tumours. The median number of sites of metastasis was two, with predominant sites being the lungs (60%), liver (39%) and bone (40%). 67% of patients have received adjuvant therapy and 38% have been given one previous course of chemotherapy for MBC; all patients have received previous anthracycline therapy. Median treatment duration with paclitaxel plus trastuzumab was 24 weeks. 49 patients are available for assessment of response and the overall response rate is 69% (n=34), including complete response in 20% of patients (n=10). The weekly regimen was generally well tolerated. The most commonly reported adverse events of grade e 2 were leucopenia (28%) and anaemia (36%). Non-haematological toxicities included myalgia, peripheral neuropathy, nausea and vomiting, which were mainly mild to moderate in severity.

Conclusions: The preliminary data are promising and suggest that the increased dose-intensity of weekly paclitaxel in combination with trastuzumab compares favourably with the reported 3-weekly paclitaxel plus trastuzumab data. Recruitment to the trial is ongoing and updated efficacy and safety data will be presented.

459 POSTER

Weekly paclitaxel: an effective and well tolerated treatment for advanced breast cancer

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Backgound; Paclitaxel has shown to be an active single agent in the treatment of metastatic breast cancer with response rates over 60% as first-line and up to 30% as second line therapy. However, the treatment is mostly palliative and thus the treatment should be as mildly toxic as possible and be convenient to patients. Therefore we initiated this national multi-institutional study with weekly paclitaxel in patients with metastatic breast cancer.

Patients and methods: Ninety-one patients (pts) progressing either after hormonal (42%) or cytostatic treatment (57%) for advanced breast cancer were included into this study. For 44% of pts weekly paclitaxel was first line, for 42% second and for 13,6% third line cytostatic treatment for advanced breast cancer. The median age of the pts was 53.8 years (range, 34-74). Twenty (22%) were pre- and 71 postmenopausal (78%). Thirty-five (38.5%) had lung and 47 (51.6%) liver metastases (mts) and 42 (46.7%) bone mts. Only 15 (16.5%) had skin mts and four (4.4%) had ascites. Fifty-eight pts (63.7%) had >1 metastatic sites. Patients should be ambulant. They should have measurable or evaluable disease and sufficient renal, liver and bone marrow functions. Brain metastases were excluded.

Treatment schedule Paclitaxel, 90 mg/m^2 with dexamethasone premedication, was given weekly i.v. three times. The treatment cycle was 4 weeks. Median of 5 cycles (range 1-13) was delivered. Four pts received only one cycle and 30 pts over 6 cycles.

Results: Ten complete (11.6%) and 37 partial (43%) responses were achieved giving an overall response rate of 54.6%. Twenty-seven stable (30.5%) and 13 progressive (15.1) diseases were recorded in 86 evaluable patients. Median time to progression was 7.5 months (range 6.5-8.5 mo) and median survival time was 20.1 months (range 13.7-26.5 mo) The treatment was in general well tolerated. Grade 3-4 neutropenia occurred in 13.3% of pts, but only 2 grade 3 and one grade 4 septic episodes were recorded. No grade 3-4 thrombocytopenia and only one grade 3 anaemia were recorded. Grade two alopecia occurred in 79.8% of the pts and neuropathy grade 1 in 41.6%, grade 2 in 16.9% and grade 3 in 11.2% of pts. Only one patient had severe myalgia/artalgia. Treatment was stopped due to progression in half of the patients and due to patients' wish in 16.9% and due to toxicity in one third of the pts.

Conclusion According to this second largest study published of weekly paclitaxel it is concluded that weekly paclitaxel is an effective and well tolerated treatment for advanced breast cancer yielding response rate 55% with a median survival of 20 months.

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Reduction of the incidence of central nervous metastases in patients treated with high dose epirubicin and high dose cyclophosphamide compared to high dose epirubicin alone for metastastic breast cancer.

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Background: Central nervous metastases (CM) occur frequently in patients (pts) with metastatic breast cancer.

Material and methods. Data from 116 antracycline naive pts with metastastic breast cancer were retrieved. All entered a phase III trial between January 1992 to November 1995, comparing (A) epirubicin 130 mg/m^2 (59 pts) every three weeks, with (B) epirubicin 130 mg/m^2 and cyclophosphamide 2500 mg/m^2 (57 pts) alternately every three weeks for a total of eight cycles as first line chemotherapy for metastatic breast cancer. Distribution of pts with lung or liver metastases, oestrogen receptor status, number of metastastic sites, and pre-treatment lactate dehydrogenase level in (A) and (B) was all identical. Retrospectively pts with CM has been listed. Statistical analyses included Kaplan-Meiers plots, Log rang test and Chi-square test.

Result. Twenty six (22%) of all pts developed CM; twenty (34%) treated with (A), and six (11%) with (B), p=0.0058. Median time to CM: (A) 20 mths (8-87 mths), (B) 7 mts (3-18 mts). Median survival: (A) 20 mths (2-92+ mths), (B) 22 mths (0-110+ mths), p-value = 0.6330. The median survival for CM pts after the CNS diagnosis: 2 mts (0-33 mts). The follow-up time was 108 mts (0-110+ mts). In CM pts response status after treatment was; CR 4 (15%), PR 10 (39%), NC 10 (39%), and PD 2 (7%).

Conclusion. Treatment with high dose epirubicin alternately with high dose cyclophosphamide reduces the incidence of CNS metastases significantly, but whitout any influence on the survival.

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Oral capecitabine monotherapy in taxane & anthracycline pre-treated metastatic breast cancer (mbc): Suffolk Oncology Centre experience

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Background: Therapeutic options in taxane & anthracycline pre-treated mbc patients (pts) are limited. Capecitabine, an oral fluoropyrimidine prodrug has shown activity in MBC. We present our experience with oral capecitabine as monotherapy in taxane and anthracycline pre-treated mbc pts from Suffolk Oncology Centre.

Material and Methods: 26 pts with mbc, (25 females and 1male) mean age 50 yrs (range 31-64 yrs) WHO PS 0-2 were treated with oral capecitabine monotherapy from 1999-2002. Informed written consent was obtained prior to treatment. All pts had taxanes (paclitaxel or docetaxel) for mbc prior to capecitabine. 14/26 had 2 or more chemotherapy regimes for mbc. Her-2neu status: 4+ve, 10ve, 12 unknown. ER status: 13+ve, 4 ve 9 unknown. Sites of metastases: Soft tissues 14/26, Liver 10/26, lung 8/26, bone 13/26 and brain 3/26. 62% had 2 or more sites of metastases. Capecitabine dose/schedule was 2.0-2.5 gm/m2/day for 14 days, given three weekly. Median number of cycles 4.5 (range 1-13). Response was assessed as per WHO criteria and toxicity as per CTC grading.

Results: 25 pts were assessable for response and 26 pts for toxicity. Overall response rates (ORR): complete response (CR) 0, partial response (PR) 25% (95% CI 8-42) and stable disease (SD) 40% (95% CI 18-62). 5/16 and 3/16 best responses were in soft tissues and liver, respectively. Overall survival: (from start of capecitabine) median 5.25 months and mean 6 months (95% CI 4.6-7.4). Time to progression: median 3 months, mean 3.4 months (95% CI 2.1-4.8). Toxicity 25% had grade 3 toxicity (palmar plantar erythema 3 pts and diarrhoea 2 pts), 60% had grade 2 or more fatigue and only 13% had grade 2 anemia. There were no neutropenic septic events or treatment related deaths.

Conclusions: Post taxane mbc has a poor prognosis. Oral capecitabine monotherapy has activity in this subgroup with ORR of 25% and SD of 40%. The best responses were achieved in soft tissues. Oral capecitabine is well tolerated with acceptable toxicity profile in this population.