PP-7-5 Phase II Study of Paclitaxel (P) and Epirubicin (E) as First-Line Therapy in Patients (PTS) with Metastatic Breast Cancer (MBC)

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In several studies the combination of P with Doxorubicin (D) showed high activities of 63–94% in pts with MBC, but severe cardiotoxic events were reported. We present preliminary data of the evaluation of P combined with E, the 4-epimer of D with lower cardiotoxic effects, in pts with previously untreated MBC. Pts were treated with 2 doses of E (group A: 60 mg/m^2; group B: 90 mg/m^2), 1 h, IV, followed by 175 mg/m^2 P, 3 h, IV, after standard premedication. Left ventricular ejection fraction (LVEF) was monitored every second cycle. Of 83 recruited pts to date 44/57 pts with 302 cycles (group A) and 19/26 pts with 91 cycles (group B) could be evaluated for response and toxicity. The main toxicity in both groups was *neutropenia* with a higher incidence of WHO III^0 + IV^0 in group B: A: WHO 0^0-II^0: 27%, WHO III^0 + IV^0: 73%; B: WHO 0^0-II^0: 2%, WHO III^0 + IV^0: 98% (2 febrile episodes). No non-hematological toxicity WHO > II^0 except for *alopecia* (A: WHO I^0 + II^0: 15%, WHO III^0 + IV^0: 85%; B: WHO I^0 + II^0: 20%, WHO III^0 + IV^0: 80%) was observed. Up to now no significant alteration of LVEF or case of cardiotoxic events could be observed. The response rates were: A: CR: 6 pts (14%), PR: 22 pts (50%), SD: 13 pts (30%), PD: 3 pts (6%); B: CR: 2 pts (14.3%), PR: 10 pts (71.4%), SD: 2 pts (14.3%). This study confirmed the efficacy and tolerability of P 175 mg/m^2 in combination with E 60 or 90 mg/m^2 in pts with MBC. The overall response rates were 64% (A) and 85.7% (B). A phase III study comparing the combination P/E to E/cyclophospamide in the first-line treatment of MBC is planned.

PP-7-6 Dose Dense Epirubicin (E) and Paclitaxel (P) with G-CSF in Metastatic Breast Cancer (MBC)

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E and P are very effective drugs in the treatment of breast cancer. If supported by haematopoietic growth factors, the dose-intensity of the EP combination may be increased. This may be accomplished by reducing the intercyclic interval. To date we treated 29 patients, without prior chemotherapy for MBC, in a multicenter phase I/II study. Treatment regimen consisted E 75 mg/m^2 (push) followed by P 135 mg/m^2 (3 h) in combination with G-CSF (5 mcg/kg). Cohorts of at least 6 patients. Further interval shortening if < 50% of patients per cohort encountered a dose-intensity limiting criterium (DILC) in cycle 1–3: stomatitis, neurotoxicity or allergy grade 3/4, neutropenia of < 500/mm^3 for > 7 days, febrile neutropenia, thrombocytopenia of < 25.000/mm^3 for > 4 days, cardiotoxicity, non-haematological toxicity grade 4, or delay of next scheduled cycle due to myelosuppression or persistence of non-haematological toxicity grade ≥ 2 (WHO-grading).

Initial DILC in cycle 1–3: In q14 days 2 DILC's occurred in 1 out of 6 pts (platelet recovery and cardio-toxicity). In q12 days (8 pts) no DILC's. In q10 days 1 DILC (ANC recovery) occurred in 1 out of 9 pts. In q8 days 4 out of 6 patients encountered a DILC (3 ANC recovery and 1 febrile neutropenia). At this moment we are investigating EP 75/175 mg/m^2 q 10 days. *Conclusion:* In combination with G-CSF, EP 75/135 mg/m^2 q10 days could be safely administered, allowing a dose intensity of E 52.5 and P 94.5 mg/m^2/week.

PP-7-7 Taxol. (Paclitaxel), Epirubicin and Cyclophosphamide (TEC) in the Treatment of Metastatic Breast Cancer (MBC): Preliminary Results of a Phase I Study

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This prospective phase I study evaluates the toxicity of polychemotherapy combining Paclitaxel (T) (1-hr. infusion), Epirubicin (E) and Cyclophosphamide (C) in patients (pts.) with MBC. Pts. are treated in cohorts of 6 with dose escalations of T as follows: DL1:135 mg/m^2; DL2:175 mg/m^2; DL3:200 mg/m^2; DL4:225 mg/m^2. E and C are given at fixed doses, 50 mg/m^2 and 500 mg/m^2 respectively. Treatment is given every 3 wks. (maximum of 10 courses) without dose escalation within cohorts. Twenty-three pts. without previous anthracycline exposure, median age 47 years (30– 66) were accrued so far in this study: 36 courses were delivered at DL1 (6 Pts.), 32 courses at DL2 (6 Pts.), 18 courses at DL3 (7 Pts.) and 6 courses at DL4 (4 Pts.).

Dose limiting toxicity has not yet been reached. Median WBC nadir was respectively 1.5, 2.1 and 1.9 × 10^9 for DL1, DL2 and DL3 (Median neutrophil nadir respectively 0.6, 0.45 and 0.36 × 10^9 with 2 episodes of febrile neutropenia). There was no thrombocytopenia or anemia. Excluding alopecia, non-hematological toxicity was mild except 1 pt. experiencing grade 4 nausea/vomiting. Cardiac toxicity was as follows: 3 Pts. with reversible drop in left ventricular ejection fraction (MUGA scan): 1 pt. at DL1 after 8 courses; 1 pt. at DL2 after 8 courses; and 1 at a DL3 after 5 courses of TEC. A case of reversible cardiomyopathy was observed in 1 Pt. after 1 dose at DL4. These preliminary results suggest that caution be exercised before further escalating doses of this combination.

POSTER PRESENTATIONS

PP-7-8 Hexadecyl Phosphocholine in the Topical Treatment of Skin Metastasized Breast Cancer

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Breast skin metastases represent a significant therapeutic problem in Medical Oncology, specially in situations where further standard measures are no longer applicable.

A total of 20 patients with skin metastases from breast cancer entered a phase 2 study of Hexadecyl Phosphocholine (Miltefosine solution 6%). The study included 18 females and 2 males. All patients were treated with up to 4 standard treatment modalities (surgery, radiotherapy, hormone and chemotherapy). With regard to predominant extended ulceration of skin lesions, (improvement) was introduced as response category to characterize a favourable clinical and subjective change of the lesion quality. Improvement (documented by photography), has been achieved in 7/17 (41%) patients from 7 up to 26 weeks. Moreover, in 4/17 (23.5%) patients a stabilization (NC) from 9 up to 39 weeks has been observed 3/20, were excluded from efficacy analysis Miltefosine solution, was generally well tolerated. In all patients, local irritation, dry skin, discharge, local pain after Miltefosine application or bleeding at ulcer have been observed. The overall tolerability has been judged as (good/very good) in 10/20 or as (sufficient) in 9/20 cases. Moreover, drug levels of all patients included in the study were not above the limit of detection. 7/17 patients derived from Miltefosine therapy a palliative benefit with a duration up to more than 6 months.

PP-7-9 Weekly Vinorelbine (VRB) as Single Agent for Advanced Breast Cancer (ABC)

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The main objective of this abstract is to value the activity and toxicity of the VRB as 4th line chemotherapy for patients afflicted by ABC. Since December 1994 up to February 1996, 14 post-menopausal women, at the end of the 3th line of therapy, have been treated with VRB 25 mg/m^2 i.v. one day weekly. Predominant metastatic sites were: lung (7), bone (3), brain (2), liver (1), soft tissue (1). All the patients have been valuable for the response and toxicity. The dose intensity was 100% in 10/14 (72%) and 80% in 4/14 (28%). Have been observed the following results: 1 CR; 8 PR; 3 NC; 2 PD. The median disease-free survival has been 6–8 months. The toxicity has been: leukopenia (G 4: 2 pts), nausea and asthenia (G1–2) in all the patients. In short, the weekly VRB as single agent for the 4th line chemotherapy has been active and well tolerated. Leukopenia, well controlled with rHuG-CSF, has been the only dose-limiting toxicity.