activities, has been used for the treatment of postmenopausal symptoms. In this paper we report the antitumor effects of OD14 treatment in rats bearing DMBA induced mammary tumors. In the 1st experiment, treatment was started when the average tumor burden was about 290 mm^2. Treatment with 1 mg/kg/2xd/po OD14 for 3 weeks resulted in 491 ± 163 mm^2 vs 1743 ± 354 mm^2 tumor burden of control rats ($p < 0.005$, $n = 8$). The effectivity of OD14 is confirmed by significantly less tumor weight: 6.1 ± 2.1 g vs 23.3 ± 7.3 g of control rats. Cumulative results of 4 experiments showed that OD14 treatment resulted in 182 ± 25% increase vs 463 ± 57% of tumors grown in control rats ($n = 32$, $p < 0.03$). In another experiment the antitumor effect of OD14 was compared with those of tamoxifen. 2 mg/kg/2xd/po, the antiprogestin Org31710 1 mg/kg/2xd/po, and in combination. After 3 weeks, tumor burden of control group was 1070 ± 290 mm^2, OD14 group was 358 ± 117 mm^2, tamoxifen group was 463 ± 283 mm^2, Org31710 group was 409 ± 145 mm^2, combined OD14 & tamoxifen group was 266 ± 139 mm^2 and of OD14 & Org31710 group was 208 ± 132 mm^2. Treatment with OD14 was shown to be as effective as treatment with either tamoxifen or Org31710; combination therapies were clearly better then treatment with single agent; they even resulted in reduction of tumor burdens. These results indicate that OD14 has no stimulatory but an inhibitory effect on DMBA induced mammary tumors.

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PP-7-16 Cardioxane Still Induces Effective Cardioprotection in Anthracycline Pretreated Breast Cancer Patients

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Cardioxane (dexrazoxane) is a cardioprotective agent which demonstrated cardioprotection in patients treated prospectively by anthracyclines (Speyer et al., *J Clin Onc* 1992, Vol 10: 117–127). Cardiotoxicity may be the limiting factor for the treatment of patients where reintroduction of anthracyclines is considered.

A retrospective analysis of all the available data (62 pts) from clinical studies with Cardioxane in breast cancer patients pretreated with anthracyclines was performed. All patients had received ≥ 100 mg/m^2 of doxorubicin or equivalent doxorubicin.

30 pts had been treated previously for metastatic disease: mean age 48 (32–64). Among them, 14 (47%) had received a cumulative dose of ≥ 300 mg/m^2 of doxorubicin. They received second line treatment with anthracyclines + Cardioxane up to 400 mg/m^2 (5 pts), 400–600 mg/m^2 (15 pts), 600–800 mg/m^2 (4 pts) > 800 mg/m^2 (6 pts).

32 patients had received previous adjuvant anthracycline treatment: mean age 54 (32–64). Among them, 65% had received ≥ 200 mg/m^2 anthracyclines. They received second line treatment with anthracyclines + Cardioxane up to 400 mg/m^2 (5 pts), 400–600 (14 pts), 600–800 (9 pts), > 800 mg/m^2 (4 pts).

Only 4 pts presented cardiac events and none presented clinical signs of heart failure, which is far less than expected in patient with high cumulative dose without cardioprotection. Other toxicities were similar to those observed in the usual anthracyclines treatment: grade 3 + 4 toxicities were: Nausea-vomiting (23%), mucositis (4%), alopecia (74%), anemia (13%), leucopenia (64%), thrombopenia (26%).

12 patients were not evaluable for response. Response rate in evaluable patients was 4% CR, 14% PR in second line treated metastatic patients; 4% CR, 50% PR in adjuvant pretreated patients. These response rates are similar to those reported in identical patients groups.

In conclusion, Cardioxane is an effective cardioprotective agent in anthracycline pretreated breast cancer patients allowing anthracycline reintroduction without compromising anticancer treatment efficacy.

PP-7-17 Paclitaxel and Carboplatin with G-CSF Support in Advanced Breast Cancer Resistant to Anthracyclines

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Paclitaxel at the dose of 200 mg/m^2 as 3-hour infusion and Carboplatin at 7 AUC with G-CSF support was given to patients (pts) with advanced breast cancer resistant to anthracycline or mitoxantrone containing chemotherapy. Treatment was to be repeated every 28 days and G-CSF was administered from day 3 to 13. Pts had to have measurable or evaluable disease and only one previous treatment for metastatic disease. As of January 1996, 32 pts with a median age of 55 (range 36–69) and a performance status of 1 (range 0–2) entered the study. 17 pts had previous hormonal treatment, 21 presented with 2 or more metastatic lesions and 21 with visceral disease. A total of 121 courses has been delivered. Eighty-five percent of cycles was given at full dose and 98% of them on schedule. Grade 3–4 toxicities included leucopenia-neutropenia (19%), thrombocytopenia (15%), infection (9%) and neuropathy (3%). So far, 2 (6%) pts demonstrated a complete and 6 (18%) a partial response. There was one toxic death due to infection. In conclusion, this combination can be given on an outpatient basis and is well tolerated and effective for pts with advanced breast cancer previously treated with anthracyclines. The study is still open.

PP-7-18 Paclitaxel Combinations with Weekly High Dose 5-FU/Folinic Acid and Cisplatin in the Treatment of Metastatic Breast Cancer — There is a Possible Role of Combining Paclitaxel with Anthracycline Non Cross Resistant Chemotherapeutic Agents in the First and Second Line Treatment I

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Introduction: Based on the results of a phase II study with a weekly (x6) schedule of a 24 h infusion of high dose 5-FU/Folinic acid (HDFU/FA) demonstrating high efficacy (RR 41%, 13/32 pts) and low toxicity in intensively pretreated metastatic breast cancer patients (pts), we added Paclitaxel (P) to HDFU/FA in a phase I/II trial. P was chosen because of its activity in pretreated metastatic breast cancer pts, different mode of action than HDFU/FA and the lack of overlapping hematologic toxicities between the combination partners.

Treatment: Pts were treated with HDS-FU (24 h infusion)/FA (2 h infusion prior to FU) weekly for six weeks (d1, 8, 15, 22, 29, 36) and P (3 h infusion) was administered additionally on day 1 and day 22. Each cycle comprised of six weeks followed by two weeks rest. All pts were treated as outpatients using i.v. port systems and portable pumps. During Phase I we chose the following dose levels (dl): Fixed doses of FA dl 1–4 500 mg/m^2 followed by HDFU 24 h infusion dl1: 1.5, dl2: 1.8, dl3 and dl4: 2.0 g/m^2. 3 h inusion of P, given prior to HD5-FU/FA, on d.1 and d.22 dl1–dl3: 135, dl4: 175 mg/m^2. Dl4 was chosen to be further evaluated during phase II.

Patient Characteristics: 51 pts entered this ongoing trial during phase II. Up to now 48 pts were evaluable for response and toxicity. Age 47 yrs (26–63), WHO PS 1 (0–2), metastatic disease sites 2 (1–4). All pts had bidimensionally measurable disease.

Pretreatment: Pts had adjuvant chemotherapy 17/51, prior chemotherapy for metastatic disease 12/51, chemotherapy both adjuvant and for metastatic disease 22/51; prior treatment with anthracyclines 34/51, resistance to anthracyclines with disease progression while treatment prior to study entry 29/51.

Toxicity: (n = 51). 153 treatment cycles at dl4 had the following toxicities (WHO grade) in (n) cycles: leucopenia 3°/4° (28); mucositis 2° (49); diarrhea 2° (35), 3° (15); hand-foot syndrome 1° (85); PNP 1° (41); nausea/vomiting 2° (37); myalgia 1° (66).

Results: (n = 48). CR 4% (2/48), PR 58% (28/48), SD 34% (16/48), PD 4% (2/48). RR (Response rate) 62%, 95% confidence interval 48–76%. Response concerning 29 patients with anthracycline refractory disease (26 pts were evaluable for response so far): RR 58% (15/26), 95% confidence interval 38–78%. Time to maximum response 2 months (1–5), remission duration 8+ months (2–11).

Conclusions: The combination of P with weekly HDFU/FA is well tolerated and indicates high efficacy also in anthracycline refractory metastatic breast cancer. In an ongoing phase II study we estimate the value of the addition of cisplatin to the regimen in the first line treatment of metastatic breast cancer.