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Vinorelbine and paclitaxel in advanced breast cancer

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Purpose: to assess the activity and toxicity of a time-intensified regimen with Paclitaxel and Vinorelbine, a phase II study was designed of Paclitaxel 135 mg/m^2, 3 hrs i.v. infusion and Vinorelbine 25 mg/m^2, i.v. bolus, administered every 15 days for 6 courses with granulocyte colony stimulating factor (rHuG-CSF) support.

Methods: 32 patients (pts) with advanced breast cancer (ABC) have been enrolled. Pt characteristics: median age 57 years (range 37–75); median ECOG PS 0 (0–3); prior cytotoxic treatment for ABC 19 pts (59%); prior anthracycline containing chemotherapy for advanced disease 16 pts (50%); dominant site of disease: viscera 20 (62%), bone 6 (19%), soft tissue 6 (19%).

Results: an overall number of 159 cycles was given (median 6, range 1–6). Objective response rate was 41% (13/32 pts) (CI 95%: 23.6%–57.6%) with 3 CR and 10 PR. Patients pre-treated with anthracyclines for metastatic disease had a response rate of 56% (9/16 pts). Response rate according to dominant site was: soft tissue 4/6 pts (66%), bone 0/6, viscera 10/20 (50%). Median duration of response was 6.2 months (range 3–18). Grade 3 and 4 toxicities were alopecia 32 pts (100%), neutropenia 4 (12%), constipation 3 (9%), thrombocytopenia 1 (3%), mucositis 2 (6%).

Conclusion: results from this trial show that the time-intensified regimen with Vinorelbine and Paclitaxel is well tolerated and has promising activity in pts with pretreated ABC.

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Salvage chemotherapy with high-dose leucovorin (lv) and 5-fluorouracil (5-fu) 48-hour continuous infusion (ci) in combination with conventional doses of cyclophosphamide (c) in anthracycline/taxane refractory metastatic breast cancer (mbc) patients. A phase II study

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Objectives: To evaluate the activity and tolerance of high dose 5-Fu/Lv in combination with conventional doses of C as salvage chemotherapy in MBC patients refractory to anthracyclines/taxanes.

Treatment: Patients with MBC refractory to anthracyclines/anthracenedione and docetaxel/paclitaxel were enrolled. C (600 mg/m^2) was given IV bolus on day 1 and Lv (500 mg/m^2/d as a 2-h infusion) followed by 5-Fu (1.5 gr/m^2/d) over a 22 h CI for two consecutive days. C was administered every 28 days while 5-Fu/Lv every 14 days.

Results: Since October 1997, 21 pts have been enrolled with a median age of 58 years (range 39–73). The PS (WHO) was 0–1 in 18 (86%) and 2 in 3 (14%) pts. Four (19%) pts had received 1 and 17 (81%) two or more prior chemotherapy regimens. All pts were evaluable for toxicity and 14 pts for response (6 too early and 1 with non measurable bone and CNS disease). Seventy-three cycles have been administered, and the median number of cycles/pt was 3 (range 1–11). The median administered dose intensity was 100% for all three agents. Toxicity was mild; 6 pts developed grade 3/4 neutropenia with no febrile episodes, 1 pt grade 3 anemia, 1 pt grade 3 thrombocytopenia. Fatigue grade 2 and 3 was observed in 4 and 2 pts, respectively. No other grade 3 or 4 toxicity was observed. Neurotoxicity grade 2 was observed in 3 pts and diarrhea with stomatitis grade 2 in 1 pt. Three out 14 pts (21%) showed a partial response (PR), four pts (29%) stable disease (SD) and 7 (50%) progressive disease (PD). The median time to progression (TTP) was 8.5 months (range 4–11). Median survival has not yet been reached.

Conclusion: The combination of high doses 5-Fu/Lv with conventional doses of C is well tolerated and effective as salvage chemotherapy in heavily pretreated patients with MBC refractory to anthracyclines and taxanes.

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Clinical value of bone marrow micrometastases (BMM) in recurrent breast cancer patients

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Purpose: The immunocytochemical detection of BMM in cancer patients indicates the existence of clinically occult hematogenous tumor cell spread. This study was designed to investigate the potential clinical value of BMM in breast cancer patients at the time of 1ocoregional recurrence and metastatic disease.

Method: At the time of tumor relapse, we analysed bone marrow aspirates from 82 patients, 45 patients with locoregional relapse, 37 patients with metastatic relapse. Carcinoma cells were detected using monoclonal antibody A45-B/B3 directed against a common epitope of the cytokeratin (CK) polypeptides, including the heterodimers CK8/18 and CK8/19 and the APAAP technique. The median follow up time of patients was 21 months.

Results: At the time of relapse, BMM were detectable in 14% of patients (n = 45) with locoregional recurrence. These patients with micrometastatic spread more frequently progressed. In patients with metastatic disease, we found BMM in 74% of patients (n = 37). The detection of BMM correlated with a progressive and fatal course of the disease. Despite metastatic disease, only 14% of patients without BMM experienced progression, whereas in almost all cases with positive bone marrow findings we observed progressive disease.

Conclusion: The persistent presence of BMM at different stages of breast cancer development points to the existence of metastatic precursor cells among this tumor cell population. Thus, the presence of BMM seems to indicate poor prognosis.

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Treatment of advanced breast cancer with taxotere and vinorelbine (VLB) ± human granulocyte colony-stimulating factor (GCSF)

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Purpose: A phase II trial was performed to investigate the efficacy and tolerance of of taxotere, vinorelbine ± G-CSF in patients with advanced breast cancer (ABC).

Methods: 38 women with ABC were treated with an iv combination regimen consisting of taxotere (30 mg/m^2, days 1 + 8 + 15) and VLB (30 mg/m^2 days 1 + 15) ± GCSF (5 mcg/kg/d s.c.) depending on nadir granulocyte counts. Treatment courses were repeated every 4 weeks.

Results: 27 patients (pts) are presently evaluable for response and toxicity assessment. 8 pts were refractory to 1st-line chemotherapy, all others were previously untreated 9 pts were pre- and 18 postmenopausal. The median age was 57 (36 to 73) yrs, and the median WHO performance status 1 (0–2). Predominant tumour sites were visceral in 18, bone in 6, and soft-tissue in 3 pts. After a median of 5 (2–6) treatment courses, 13/19 (68%) previously untreated pts, and 518 chemotherapeutic pretreated pts had an objective tumor response, 7 had SD, and only 2 PD. The median time to response was 2.1 (1.5–4.0) months, median duration of both response and survival have not been reached yet. WHO grade 3 and 4 granulocytopenia occurred in 9 and 6 pts, and was associated with septicaemia in only 2 cases. Nonhaematologic side-effects were generally mild to moderate and included alopecia (67%), nausea/vomiting (44%), peripheral neuropathy (30%), constipation (15%), and mucositis (15%).

Conclusions: Results of this study suggest that taxotere/VLB ± GCSF is an effective and fairly well tolerated regimen for the treatment of ABC.