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Final results of a phase II study of Taxotere (docetaxel, D), doxorubicin (Dx) and cyclophosphamide (CTX) (TAC) in the treatment of metastatic breast cancer (MBC)

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We conducted a phase II study of D (75 mg/m2, 1 hour i.v. infusion) with Dx (50 mg/m2, i.v. bolus) and CTX (500 mg/m2, slow i.v. bolus) q.3 weeks for a maximum of 8 courses in patients (Pts) with MBC without prior anthracyclines or taxanes. Fifty four patients with MBC were enrolled and received 339 courses. Pts characteristics are as follows: mean age: 53 years (33–70), prior adjuvant chemotherapy (CMF): 17 Pts (32%), visceral involvement: 33 Pts (62%), bone metastases: 32 Pts (60%), more than 3 metastatic sites: 28 Pts (52%), median follow-up 14 months (9–18). Forty eight Pts are evaluable for response (median number of courses: 7). The major response rate is 79% in patients with measurable disease and 73% overall with Stable Disease in 9 Pts (19%) and Progressive Disease in 4 Pts (8%). Time to progression and survival data will be presented at the meeting. Toxicity was evaluable in 54 Pts. Neutropenia is the main toxicity (grade 4: 70%, lasting less than 7 days) with febrile neutropenia seen in 6% of courses. There was no grade 4 toxicity, while grade 3 toxicity was limited (nausea: 9.2%; diarrhea: 3.7% and stomatitis: 5.5%)). Taxotere-specific toxicity was mild with 2% severe fluid retention (no Pt discontinued for toxicity). No severe skin, hypersensitivity or nail toxicity was observed. One Pt presented with a reversible CHF (2%). TAC is a well tolerated and active regimen with no unexpected cardiac toxicity and is the base of 2 large international multicentric randomized trials comparing TAC to FAC in metastatic and adjuvant setting.

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Serum tumor markers in metastatic breast cancer comparative study between CEA, CA-15.3 and MCA

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Purpose: Tumor markers are frequently requested at the time of Breast Cancer (BC) relapse and during treatment. To compare the sensitivity of the serum tumor markers CEA, CA-15.3 and MCA for the presence of metastatic disease, we performed a cross-sectional study.

Material and Methods: One-hundred and thirty-six BC patients with advanced disease were included in the study. Serum determinations of CEA, CA-15.3 and MCA, were performed using ELISA test. CEA, CA-15.3 and MCA were considered abnormally elevated if above 2.5 ng/ml, 28 U/L and 11 U/L respectively.

Results: The three tumor markers had different sensitivity for the presence of metastatic disease ($p < 0.0000008$, Cochram Q test). CEA was the tumor marker most frequently elevated (59.8%), followed by CA-15.3 (46.4%) and MCA (35.7%). The combination of CEA and CA-15.3 had the highest sensitivity (66.1%). However, when compared with CEA plus MCA the difference didn't reach statistical significance ($p = 0.08$, McNemar test). The three tumor markers combined had the same sensitivity as CEA plus CA-15.3. Any combination of tumor markers that includes CEA, increases significantly the sensitivity when compared with CEA alone.

Tumor Markers	Sensitivity (%)	CI 95%
CEA + CA-15.3	66.1	57.2 75.0
CEA + MCA	63.4	54.3 72.5
CA-15.3 + MCA	47.3	37.9 56.7
CEA + CA-15.3 + MCA	66.1	57.2 75.0

Conclusions: In BC patients with advanced disease CEA is the single tumor marker with highest sensitivity. The combination of CEA with another tumor markers increases significantly sensitivity, suggesting that a first determination of tumor markers in BC with metastatic disease, should include CEA and another tumor marker.

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Meta-analysis of dose intensity in breast cancer neoadjuvant chemotherapy (1997 update)

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Dose intensity (DI) in chemotherapy is defined as the amount of drug delivered per unit time and is usually standardized to body surface area as mg/m2/wk. A positive relation between DI and treatment outcome has been demonstrated not only in advanced breast cancer (BC) but also in adjuvant setting. Only few trials using DI concepts have been performed in neoadjuvant chemotherapy for BC. To determine if chemotherapy DI influences treatment outcome in BC, 52 published trials (8 randomized trials included two regimens) from 1984–1997 (including ASCO-97) were retrospectively analyzed (4857 patients). Regimens included such agents as Cyclophosphamide (43 trials) or Tiotepa (1), Fluorouracil (34), Doxorubicin (28) or Epidoxorubicin (20), Methotrexate (13), and Vinca alkaloids (9, Vincristine – 7) (from single drug therapy to five-drugs combinations). Relative DI (RDI) of each study regimen was calculated against commonly used doses of each drugs in single regimens (eg, 25 mg/m^2/wk for Doxorubicin, 400 for Cyclophosphamide, 25 for Methotrexate, etc.). Meta-analysis of chemotherapy trials for BC with some various regimens have suggested that higher total RDI correlated strongly with improved response rate (51 trials, $r = 0.43$, $p = 0.0016$) and complete response (40 trials, $r = 0.42$, $p = 0.0065$). Meta-analysis demonstrated that response rate in neoadjuvant chemotherapy of BC correlates with DI. A randomized controlled trial targeted for DI itself will be necessary to confirm the usefulness of DI concepts in neoadjuvant chemotherapy in BC.

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Vinorelbine in combination with 5-fluorouracil in metastatic breast cancer (MBC)

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Between March 1996 and December 1997, 27 consecutive patients (pts) with MBC were treated with Vinorelbine 20 mg/m^2 on days 1 and 8 as a short intravenous infusion and 5 Fluorouracil 350 mg/m^2 i.v. + folinic acid 100 mg/m^2 i.v. on days 1° to 5° every three weeks. Patients characteristics: median age 56 years (range 32–73); median ECOG PS 1 (range 0–2). The sites of metastatic disease were: liver (6 pts), lung (6 pts), bone (21 pts), lymphonodes (5 pts), skin (10 pts). 15/27 pts (55%) had $\geq$2 metastatic sites; 22 of the 27 pts (81%) had received prior chemotherapy in adjuvant setting (11 with anthracycline). 14/27 (52%) pts had received prior chemotherapy for advanced disease (only one chemotherapy regimen), 8 of them with anthracycline. All pts are presently evaluable for toxicity assessment and 25/27 are evaluable for response (1 pt presented with severe cutaneous allergy after the first cycle and discontinued the treatment). A total of 126 cycles was administered (median 6; range 1–9). Overall response rate was 44% (11/25): 1 CR and 10 PR. 9 pts achieved a stabilisation of metastases and 5 progression of disease. This regimen appeared to be well tolerated with mild to moderate toxicity: nausea and vomiting grade (G) 1 and 2 in 18/27 pts (67%), peripheral neuropathy G1 in 5/27 pts (18%); diarrhea G3 occurred in 1 pt. The main toxicities (G3 and 4) were mucositis in 6/27 pts (22%) and neutropenia 14/27 pts (52%).

To conclude, the association of 5 Fluorouracil and Vinorelbine is an active and tolerable regimen for metastatic breast cancer even in anthracycline pre-treated pts.

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Early breast cancer: How long should tamoxifen continue?

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The recent overview by the Early Breast Cancer Trials Collaborative Group analysed data on – 37,000 women in 55 trials of adjuvant tamoxifen (TAM). For women with receptor positive disease, or with unknown receptor status, TAM is of substantial benefit, regardless of age or nodal status. 5 years of TAM appears better than 2 years. There is inadequate evidence on the effects of 10 compared with just 5 years of TAM. 1 million women worldwide are now on TAM, with most clinicians prescribing TAM for ~5 years. Whilst there is good reason to believe that 10 years might confer extra benefit, the balance of long-term benefits and risks must be established. Trials to