In patients who had received anthracycline-containing adjuvant CT, the cumulative doses had not to exceed 180 mg/m^2 for doxorubicin, 360 mg/m^2 for EPI, and 72 mg/m^2 for mitoxantrone. Patients received a maximum of 6 cycles.

Results: Between October 2000 and March 2002, 49 patients have been enrolled. Median age was 55 years; 88% had visceral involvement (51% liver; 37% lung) and 37% had at least 3 organs involved. The most common toxicity was neutropenia with 65% of patients with grade 3-4, 8% of febrile neutropenia and 12% of neutropenic infection. The main non haematological toxicities included nausea (86% of patients), vomiting (59%) and fatigue (77%) but they were rarely severe. No cardiac toxicity except one transient episode of arrhythmia was seen. Twenty five patients responded, yielding a response rate of 51% in the intent-to-treat population and 55% in the 44 evaluable patients. Median duration of response was 8.5 months. With a median followup of 9.5 months, the median progression-free survival has not been reached.

Conclusion: VRL alterning oral and IV in combination with EPI is an effective and convenient therapeutic option for MBC. Its activity and safety profile are similar to those reported for the fully IV regimen.

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A phase II study of first-line combination chemotherapy with docetaxel and gemcitabine in anthracycline-pretreated, Her-2 negative metastatic breast cancer (MBC)

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Background: The combination of docetaxel (D) and gemcitabine (G) is particularly attractive as both agents are not completely cross-resistant and have been shown to be active in anthracycline-pretreated MBC. This phase II study evaluated the efficacy and safety of D and G in anthracycline-pretreated patients with MBC not overexpressing *Her-2/neu*.

Materials and methods: Patients with MBC (n=36) not overexpressing *Her-2/neu* and pretreated with an anthracycline-based adjuvant or neoadjuvant chemotherapy received D 75 mg/m^2 on Day 1 and G 1000 mg/m^2 on Day 1 and Day 8 every 3 weeks as first-line chemotherapy. The predominant metastatic sites were visceral (liver 36% and lung 30%); 10 (28%) patients had soft tissue metastases and 2 (6%) patients had bone lesions alone.

Results: All patients were evaluable for toxicity and 35 for response. A total of 184 cycles were given to 36 patients (median 6 cycles, range 1-6). A complete response was recorded in 8 (23%) patients and a partial response in 11 (31%) patients for an overall response rate of 54%. With a median follow-up of 11 (range 3-22) months, median time to progression was 8 (range 2-21) months. Median overall survival has not been reached so far. The predominant toxicity was leucopenia, however, no febrile neutropenia occurred. Haematological toxicity WHO grade 1-4 occurred as follows (% of patients/% of cycles): leucopenia grade 1, 14%/22%; grade 2, 33%/34%; grade 3, 47%/30% and grade 4, 6%/2%; thrombocytopenia grade 1, 28%/14%; grade 2, 8%/2%; grade 3, 14%/3%; grade 4, 0%/0%; anaemia grade 1, 47%/34%; grade 2, 19%/6%; grade 3, 3%/1%; grade 4, 3%/1%. The most common grade 1 or 2 nonhaematological toxicities per cycle were nausea and vomiting 21%, mucositis and stomatitis 20%, diarrhoea 15%, asthenia 28%, neurological symptoms 22%, pain 22%, nail and cutaneous disorders 21%, and dyspnoea 8%. Grade 3 or 4 toxicity per cycle included dyspnoea 3%, pain 2%, asthenia 2%, nausea and vomiting 2%, and constipation 1%.

Conclusion: The D-G combination regimen was active and well tolerated as first-line treatment of anthracycline-pretreated MBC not overexpressing *HER-2/neu*.

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Caelyx (pegylated liposomal doxorubicin hcl) and conventional doxorubicin have significantly different adverse event profiles

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In a previously reported randomized, phase III trial in first-line treatment of 509 women with metastatic breast cancer, CAELYX™ and conventional doxorubicin were shown to have comparable efficacy with respect to progression-free survival. There was a significantly greater risk of cardiotoxicity with conventional doxorubicin compared with CAELYX™ (P<.001). In order to ascertain whether there were other significant differences in toxicity between the 2 agents, a post-hoc analysis was performed using data from the trial. Twenty types of adverse events were reported in ≥5% of patients in either arm. Palmar-plantar erythrodysesthesia was the most frequently reported adverse event related to CAELYX™ treatment (48% of patients overall; NCI-CTC Grade 3 in 17%, and Grade 4 in 0%), whereas alopecia was the most frequently reported adverse event associated with conventional doxorubicin, (reported in 66% of patients overall; pronounced or total hair loss reported in 54%). Adverse events related to the skin or mucosa were significantly more prevalent in the CAELYX™ arm and included mucositis (CAELYX™ = 59 events, conventional doxorubicin = 33 events; P = 0.0026), stomatitis (CAELYX™ = 55 events, conventional doxorubicin = 38 events; P = 0.0487), palmar-plantar erythrodysesthesia (CAELYX™ = 123 events, conventional doxorubicin = 5 events; P<.0001), rash (CAELYX™ = 25 events, conventional doxorubicin = 4 events; P<.0001), erythema (CAELYX™ = 18 events, conventional doxorubicin = 3 events; P = 0.0008), and abnormal pigmentation (CAELYX™ = 21 events, conventional doxorubicin = 6 events; P = 0.0029). Alopecia (CAELYX™ = 51 events, conventional doxorubicin = 169 events; P<.0001), nausea (CAELYX™ = 94 events, conventional doxorubicin = 136 events; P = 0.0002), vomiting (CAELYX™ = 48 events, conventional doxorubicin = 78 events; P = 0.0022), and neutropenia (CAELYX™ = 10 events, conventional doxorubicin = 25 events; P = 0.0089) were more often associated with conventional doxorubicin treatment. In this posthoc analysis there were no other significant differences in adverse event frequency between the 2 groups. CAELYX™ and conventional doxorubicin have distinct toxicity profiles. Skin and mucosal toxicity are the most common type of adverse events associated with CAELYX™ whereas conventional doxorubicin is associated with significantly more alopecia, nausea, vomiting, and neutropenia.

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Multicenter phase II study of sequential hormonotherapy with Anastrozol/Exemestane (ARIM-AROM) in metastatic breast disease. Preliminary data of Goim 2107 study.

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The study was oriented to evaluate the overall response as primary endpoint, TTP, clinical benefit, toxicity and overall survival as secondary end-point.

Eligibility criteria: Advanced breast cancer or primary tumour or locally advanced not resectable, with positive or unknown ER/PgR, with interrupted TMX treatment and physiological, pharmacological, radiotherapeutic or surgical menopause.

Treatment: Anastrozol 1 mg/die up to progression, followed by Exemestane, 25 mg/die up to 2nd progression.

Recruitment time: 12 months.

Patient characteristics: 99 pts were recruited, median age 67 (range 36-93) with bone metastases (55%), skin and lymphonodes (27%), liver (33%) and PS 0 (58%), PS 1 (35%), PS 2 (17%) and 42 months median DFS.

Results: 73 valuable pts; CR 5 (7%), PR 18 (24,5%), OR 23 (31,5%), NC 24 (33%), PD 21 (29%). In 18 pts treated in second line with exemestane were registered 2 PR and 4 NC >4 months.

Conclusion: These actual data are on line with literature results. Very promising seem preliminary not shown data of median response duration and clinical benefit. The next update will be at the end of June 2003.

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Weekly paclitaxel plus trastuzumab in metastatic breast cancer (MBC): a multicentre German trial

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Background: Three-weekly paclitaxel plus weekly trastuzumab therapy has proven clinical benefit in metastatic breast cancer (MBC) (Slamon D, et al. New Engl J Med 2001:344;783-92). The current trial investigates the efficacy and safety of weekly administration of both paclitaxel and trastuzumab in MBC.