(liver 51%, lung 36.7%). Neutropenia was the main side effect: gr3/4 in 65.3% of pts and 29.1% of cycles, resulting in febrile neutropenia in 8.2% and neutropenic infection in 12.2% of pts. Stomatitis gr3/4 was seen in 10.2% of pts. The combination demonstrated to be effective with RR of 51% [95% CI = 36.3–65.6], and 54.5% [95% CI = 38.9–69.6] in ITT and evaluable population, respectively. Median PFS is 8.1 months [95% CI = 6.9–9.9] with 3 pts censored. The median overall survival is not reached with a median follow up of 23.7 months. The use of NVB oral for the day 8 administration of an NVB–EPI every 3-week cycle provides good results, improves patient convenience and allows better use of resources.

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Multicenter phase II trial of three-weekly docetaxel and weekly trastuzumab in HER-2-overexpressing metastatic breast cancer patients: Japan East Cancer Center Breast Cancer Consortium (JECBC 01 trial)

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Background: Docetaxel and trastuzumab can be considered to be active drugs for HER-2-overexpressing metastatic breast cancer (MBC). This study was conducted to determine the activity of combination therapy with docetaxel and trastuzumab in MBC patients (pts) by assessing the response rate (RR), time to progression (TTP) and safety.

Material and Methods: We administered the combination of docetaxel 70 mg/m^2 every 3 weeks and trastuzumab using a 4-mg/kg loading dose and thereafter 2 mg/kg weekly for HER-2-overexpressing MBC. One cycle was three weeks.

Results: Between March 2002 and May 2003, 40 pts with HER-2-positive (3+ by immunohistochemistry 39, FISH+ 1) MBC were enrolled in this study, and 39 pts were eligible. ITT analysis was performed for 40 pts. The median pt age was 57.5 years (range, 32–73). Prior chemotherapy was anthracycline-based in 16, non-anthracycline in 17, and radiotherapy in only 1. Only 6 pts were naive. Performance status ECOG: 0/1/2/unknown (23/11/4/2). Histology: invasive/other/unknown (38/1/1). Metastatic site: soft tissue 26 (primary: 5; lymph node: 15; skin: 6), visceral 32 (liver: 13; lung: 17; pleura: 2), bone 12, and other 1. Number of metastatic sites: 1/2/3/* 4 (20/12/5/ 3). Hormone receptor status: ER+/ER− (8/32), PgR+/PgR−/unknown (10/29/1). Menopausal status: postmenopausal/premenopausal/unknown (29/10/1). The median number of cycles administered was 6 (range, 1–13+). To date, 40 pts who received at least one cycle of this combination treatment have been assessable for efficacy. The overall RR was 70.0% (28/40) [95% CI 53.5%-83.4%], with 7 CR, 21 PR, 4 SD, 3 PD and 5 NE. The median follow-up time was 230 days, while the TTP was 135 days (range, 19–443). The number of pts assessable for safety was 40. NCI–CTC grade 3–4 toxicities were leukopenia 87.5% (35/40) and neutropenia 82.5% (33/40). The main non-hematological toxicities were anorexia 55%, diarrhea 55%, asthenia 72.5%, alopecia 90%, neuropathy 55%, rash 55%, edema 60% and nail changes 57.5%. All these toxicities were grade 1–2. NCI–CTC grade 3 toxicities were weight gain in 2 patients, and neuropathy, fever and rash in one pt each.

Conclusion: The combination of docetaxel and trastuzumab was a well-tolerated and very active regimen for the treatment of patients with HER-2-overexpressing MBC. We plan to investigate the predictive value of p-53, Ki-67, ER, PgR, etc.

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A clinical phase II study of cisplatin and vinorelbine followed by docetaxel as first line treatment in metastatic breast cancer

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Background: Based on our encouraging positive experience with Cisplatin and Vinorelbine combination (PVn) in first and second line treatment for advanced breast cancer (ABC) [Am J Clin Oncol 1999; 22(3): 298–302, Proc 12th ICACT Paris, February 2002; (abstract P 97)], and to explore additive effect of sequential docetaxel, we designed this phase II study to assess anti-tumor efficacy and safety of PVn followed by docetaxel in patients with metastatic breast cancer (MBC).

Material and Methods: From August 2002 to October 2003, 27 patients with MBC were recruited of whom 26 were evaluable for response. Median age was 49 years (range: 22–75). 13 (50%) patients were premenopausal. 80% of patients had 2 or more sites of metastasis. No previous therapy was allowed except as adjuvant. 10 (38%) patients were chemo naive and 16 (62%) patients underwent previous surgery for breast cancer and received adjuvant anthracycline chemotherapy regimen. 14 (54%) patients received locoregional radiotherapy, and 10 (38%) patients received hormonal therapy. Accrual of patients is still ongoing. Chemotherapy consisted of cisplatin 80 mg/m^2 given on day 1 of a three-week cycle and vinorelbine 30 mg/m^2 on days 1 and 8 for a total of 4 cycles with evaluation every 2 cycles. After the 4th cycle responding patients received docetaxel 75 mg/m^2 on day 1 every 21 days for a maximum of 4 cycles. Hormone receptor positive patients received hormonal therapy after the end of the study. Evaluation of measurable disease was done by physical examination and appropriate computerized tomography scans.

Results: After a median follow up of 9 months (range: 1–14), 22 (85%) patients completed the study with 4 (18%) patients showed CR, and 10 (45%) patients showed PR (ORR 63%). The median time to disease progression was 4 months (range: 2–9). 85% of patients survived for 1 year. The total number of cycles was 140. Dose reduction occurred in 32/140 (23%) cycles. Anemia Grade III observed in 8 (5%) cycles, and Grade IV in 13 (9%) cycles. Neutropenia Grade III in 8 (5%) cycles, and Grade IV in 11 (8%) cycles. Febrile neutropenia observed in 8 (5%) cycles. Thrombocytopenia Grade III in 4 (3%) cycles, and Grade IV in 10 (7%) cycles. Neurotoxicity Grade IV in 4 (3%) cycles. Nausea and vomiting Grade III in 30 (22%) cycles, and Grade IV in 14 (10%) cycles. Alopecia Grade I in 41 (29%) cycles and Grade II in 17 (12%) cycles.

Conclusions: PVn followed by docetaxel produces good results in MBC with acceptable toxicity. According to our previous experience with PVn as first line therapy in MBC (ORR 64%), it seems that sequential addition of docetaxel to PVn does not produce additional benefit.

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Efficacy and safety data of an outpatient regimen for pretreated metastatic or relapsed breast cancer (MBC): Vinorelbine, 5-Fluorouracil and Folinic Acid (FuFolNav) – a phase II study

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In incurable MBC patients (pts) with an indication for chemotherapy, low toxicity outpatient regimens that do not decrease the quality of life are a better alternative than more aggressive inpatient regimens, often without large difference in efficacy. For anthracycline (A) pretreated patients, the association Vinorelbine and 5-Fluorouracil + Folinic Acid (FuFolNav) represents a potentially non cross-resistant regimen. The purpose of this study was to evaluate the efficacy and tolerability of the combination administered as an outpatient regimen to patients with prior exposure to A.

Methods: 61 pts with MBC were treated with FuFolNav chemotherapy: 5-FU 600 mg/m^2, preceded by Folinic Acid 30 mg/m^2, and Vinorelbine 25 mg/m^2, day 1 and day 8, in an outpatient clinic, every three weeks.

Patients: A total of 61 pts were enrolled. Median age was 50 [33–67]. Metastatic sites: liver 19, lymph nodes 12, lung 11, multiple 9, skin 7, peritoneal 3. In our patient population, only two pts did not have prior exposure to A. Of the other 59, 31 pts received A as primary systemic therapy for locoregionally advanced disease, 19 pts received adjuvant A chemotherapy, and the remaining 9 pts received A as first line treatment for MBC. Out of the 31 pts treated with primary A therapy, 13 also received taxanes as sequential treatment after surgery. FuFolNav represented first line chemotherapy for MBC in the majority of pts (49). The other 13 pts received prior chemotherapy for metastatic disease, either with A or with T.

Results: We recorded 2 (3.3%) CRs (one in lung metastases, the other one in skin metastases), and 34 (55.7%) PRs, for an overall response rate of 59% (0.05 CI: 47–71%). In addition 15 (24.6%) pts had SD. Ten pts (16.4%) progressed under treatment. Overall, 51 patients (=83.6%, CI: 74.6–92.6%) had clinical benefit quantified as PR+SD and palliation of symptoms. A total of 268 cycles of FuFolNav were administered, with a median 4 cycles per pts (range 2–10). Toxicity was mild and there were no toxic deaths. Grade 3–4 toxicities included neutropenia (8%), ileus-like syndrome (6%), mucositis (5%) and peripheric neurologic toxicity (limbs) (4%) of cycles. No patient developed complete alopecia.

Conclusion: The combination of Vinorelbine, 5-Fluorouracil and Folinic Acid proved to be efficacious in the treatment of MBC pts previously