(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

exposed to A. The low toxicity of the FuFolNav regimen allowed safe administration in the outpatient setting.

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Bisphosphonates in metastatic breast cancer

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Background: The use of bisphosphonates is an essential in the treatment of patients with osteolytic bone metastasis of breast cancer. The guidelines of the American Society of Clinical Oncology recommends the administration of bisphosphonates each 3–4 weeks continuously until impairment in the performance status.

We analyze the therapeutic results and adverse effects of bisphosphonates in breast cancer patients with bone metastases.

Material and Methods: from October 1997 until February 2002 we studied 178 patients treated with Pamidronate 90 mg IV given in 60 minutes each 3–4 weeks. After that date, we administered Zoledronic Acid 4 mg IV in 15 minutes, to all the patients, but this is not the endpoint on this report. We analyzed the age, metastatic location, number of administrations, adverse effects and the number of skeletal complications along the time that the drug was given. All the patients received concurrently chemotherapy, hormonal therapy and/or radiotherapy if it was needed. Bisphosphonates were given until it was an important decreased in performance status.

Results: All the patients were diagnosed of breast cancer with bone metastases. The median age was 55.6 years old (range 29–81). A total of 17.4% of patients had only one metastatic lesion. The average of administered cycles were 10 (range 3–62), and the average accumulated dose was 900 mg (270–5580 mg). A 48.3% (86) of the patients received treatment continuously at least for 2 years. We analyzed the calcium and creatinine serum levels. A total of 2.5% of the patients developed an analytic hypocaliemia (Ca<8 mg/dl) without symptoms. We had no events of renal failure or creatinine levels >2 mg/dl. The percentage of skeletal-related events is 20.8% and a total of 33.1% need radiotherapy treatment simultaneously. Pain, evaluated by a visual analogic scale (VAS) is decreased in these patients but there are many factors that contribute to these results. Breakthrough pain was reported only in 12% of the patients with a level of VAS superior to 5. A total of 6.18% (11) related an increase of pain after the first cycle of bisphosphonates and a total of 14.6% (26) referred an acute phase reaction of bone pain fever arthralgias and myalgias.

Conclusion: Bisphosphonates improve the intensity of pain in patients with breast cancer and bone metastases, and decrease the episodes of breakthrough pain. The adverse effects are presented in a small proportion and are slight and transitory. In our series we have no events of renal failure. The skeletal-related events are small when compared with historical controls. It can be administered simultaneously with chemotherapy hormonal therapy and radiotherapy without relevant clinical problems.

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Results of a phase II study of liposomal doxorubicin (Myocet®) in combination with weekly paclitaxel and trastuzumab (Herceptin®) in patients with HER2-positive locally advanced or metastatic breast cancer (LA/MBC)

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Background: The pivotal trial (H0648g) in patients with HER2-positive MBC demonstrated that first-line trastuzumab (Herceptin®) plus doxorubicin was efficacious, but associated with an increased risk of cardiotoxicity compared with doxorubicin alone. Myocet®, a liposome-encapsulated form of doxorubicin, is as effective as doxorubicin in MBC, but is associated with less cardiac toxicity. Following promising results from a phase I dose-finding study (n=21), in which the combination of Myocet®, Herceptin® and paclitaxel produced a high response rate with very low cardiac toxicity, this combination was investigated further in this phase II study.

Materials and methods: Patients with HER2-positive (IHC 3+/FISH+) LA/MBC (previously untreated) were eligible for this study. Treatment consisted of Myocet® 50 mg/m^2 every 3 weeks $\times$6, weekly paclitaxel 80 mg/m^2 and Herceptin® 2 mg/kg, given for 52 weeks for LA and until disease progression for MBC. Cardiac function was assessed every 3 weeks and tumour response every 6 weeks during therapy. The primary endpoint was response rate.

Results: A total of 54 patients were included; 30 patients had LA and 24 MBC. Of these, 52 patients have been evaluated for response (29 with LA and 23 with MBC). The ORR is 92.3% (CR 25, PR 23), a further 4 patients had stable disease. The response rate in patients with LA was 93.1% (CR 20, PR 7) and in patients with MBC 91.3% (CR 5, PR 16). Neutropenia was the most common grade 3–4 event, with 12 episodes of febrile neutropenia. Other toxicities included alopecia, nausea, vomiting, hand–foot syndrome and ungueal toxicity. Three patients had decreases in LVEF to below 50%, with no cases of symptomatic heart failure.

Conclusions: In women with HER2-positive LA/MBC, the combination of Myocet® with paclitaxel and Herceptin® is highly active and well tolerated, with no unexpected toxicity.

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Renal safety of ibandronate in patients with bone metastases from breast cancer: phase III trial results

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Background: Increasing awareness of the nephrotoxic potential of certain intravenous bisphosphonates that are used to manage metastatic bone disease has led to recent publications [1–4] and modification of the prescribing information. Patient management would be simplified by availability of a bisphosphonate that does not have significant renal safety issues. Ibandronate is a highly-potent aminobisphosphonate that has recently been approved for the prevention of skeletal events in patients with breast cancer and bone metastases. In this context, the renal safety of ibandronate given intravenously and orally has been examined in multicenter, randomized, double-blind phase III trials over 96 weeks of treatment, supporting a difference versus other intravenous aminobisophosphonates.

Methods: In a trial of intravenous ibandronate, patients were randomized to a 6 mg dose (n=154) or placebo (n=158) infused over 1–2 hours every 3–4 weeks. In two oral studies (data pooled), patients received ibandronate 50 mg (n=287) or placebo (n=277) once daily. Renal adverse events (AEs) and serum creatinine levels were monitored throughout the study period.

Results: The percentage of patients with renal AEs or increased creatinine levels was low and similar between the intravenous ibandronate 6 mg and placebo groups (4.0% versus 4.5%; 2.6% versus 1.3%, respectively). None of the renal AEs with intravenous ibandronate were graded serious, or led to withdrawal from treatment. The incidence of renal AEs with oral ibandronate 50 mg was also comparable to placebo (5.2% versus 4.7%). Elevated serum creatinine levels were observed in 1.4% of patients in the oral ibandronate group and 2.2% of patients in the placebo group.

Conclusions: Intravenous and oral ibandronate have renal safety profiles that are comparable to placebo in patients with metastatic bone disease from breast cancer. As stated in the product labelling, ibandronate may be used in patients with existing renal function impairment and patients taking nephrotoxic medications; and serum creatinine monitoring is at the clinician's discretion (not required prior to each dose).

References

[1] Rosen, LS et al. Cancer J 2001;7:377–87.
[2] Chang JT, et al. NEJM 2003;349:1676–9.
[3] Stein SH, et al. Proc ASCO 2003;22:46 (Abstract 2997).
[4] Banerjee D, et al. Am J Kidney Dis 2003;41:E18.

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Fulvestrant in postmenopausal women with metastatic breast cancer progressing on prior endocrine therapy – results from an expanded access programme

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Background: Fulvestrant ('Faslodex') is an estrogen receptor (ER) antagonist with no agonist effects. Fulvestrant downregulates the ER, which leads to reduced cellular levels of progesterone receptor (PgR). This abstract reports the results of an expanded access programme (supported by AstraZeneca) in which postmenopausal women with metastatic breast cancer whose disease had progressed on prior endocrine therapy were treated with fulvestrant 250 mg.

Methods: Fulvestrant 250 mg was given as a single 5 mL intramuscular injection, once every 28 days until disease progression or