as first site of recurrence. Thirty-seven percent of pts received taxol and 39% herceptin based regimens before cerebral relapse occurred. Among 81 pts with known hormone receptor status of their primary tumour, 42 (52%; 95%CI: 41–63%) had oestrogen and progesterone receptor negative tumours. C-erbB2 overexpression was identified in 38 of 78 assessed tumours (49%; 95%CI: 37–60%). These figures are significantly different from those expected in the general population of pts with breast cancer, where about 30% of cases are ER-/PgR-negative and roughly 25% show c-erbB2 overexpression ($p < 0.001$ for both comparisons, exact binomial test).
Conclusions: Pts with non endocrine responsive and Her-2/neu over-espressing disease may be considered at higher risk of brain relapse. In these subsets of pts screening and prophylactic measures should be investigated.

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The significance of chemotherapy in the treatment of carcinomatous meningitis in breast cancer patients

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Introduction: Carcinomatous meningitis is a severe and progressive cancer metastasis caused by infiltration of the leptomeninges and the cerebrospinal fluid by cancer cells.
Purpose: The aim of the study was to establish if systemic chemotherapy applied after intrathecal treatment and radiotherapy can influence on survival period in patients with breast cancer carcinomatous meningitis.
Materials and methods: 53 patients with breast cancer and carcinomatous meningitis were treated in Cancer Center, Warsaw, between 1999–2005. Three methods of treatment were applied: intrathecal treatment, intravenous systemic chemotherapy and radiotherapy. Intrathecal methotrexate, 10 mg per dose, was performed in 89% patients. 30% did not respond after 1–2 courses of treatment and in these cases palliative treatment was continued. The others continued treatment. An average of 6 cycles (1–15) was administered; initially metothrexate twice a week and after clinical improvement the treatment was continued once a week until the normalization of the cerebrospinal fluid, however not more than 15 intrathecal injections.67% women received systemic chemotherapy concurrently with intrathecal treatment. Individual schedules of systemic treatment were used, but the most common were vinorelbine with fluorouracil, antracyclines, cisplatin, taxanes, trastuzumab and capecitabine. 59% patients received radiotherapy to the brain or spinal cord.
Results: Clinical and laboratory response was achieved in 67% patients. The mean survival since diagnosis of carcinomatous meningitis was 18 weeks (1–80 weeks).
In severe condition patients (Karnofsky <60%) who were not treated the median survival period was 4 weeks and after chemotherapy treatment was prolonged to 18 weeks. In not treated patients with Karnofsky above 60% the median survival period was 12 weeks. After systemic chemotherapy it was prolonged to 20 weeks. Log rank test stratified for Karnofsky status was highly statistically significant ($p < 0.001$).
Conclusions: Our observations suggest, that systemic chemotherapy added to intrathecal treatment and radiotherapy is an important factor improving survival in breast cancer patients with carcinomatous meningitis.

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Long-term safety of intravenous ibandronate throughout 4 years of treatment for metastatic breast cancer

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Background: Despite their widespread use in metastatic bone disease, some intravenous bisphosphonates are occasionally associated with renal toxicity, which may lead to discontinuation of supportive care as well as anticancer medications. Ibandronate is a non-cyclic, single-nitrogen bisphosphonate with a renal safety profile comparable with placebo that is highly effective against skeletal complications and metastatic bone pain. Here, we present safety data from a study of intravenous ibandronate over a 4-year period.
Materials and methods: During an initial 2-year study, breast cancer patients with bone metastases (n = 62) were treated with placebo (n = 16) or ibandronate 6 mg (n = 46) by intravenous infusion over 1–2 hours every 3–4 weeks. In a 2-year extension phase, all patients received active treatment but were classified according to their initial treatment (placebo/6 mg and 6 mg/6 mg groups). Safety was assessed by adverse event (AE) reports and clinical laboratory evaluations. Data from the initial (Years 1–2) and extension (Years 3–4) phases of the study were analyzed separately.
Results: During the initial study, 56.3% of placebo- and 67.4% of ibandronate-treated patients reported treatment-related AEs, compared to 6.3% of the placebo/6 mg group and 13.0% of the 6 mg/6 mg group during the extension phase. All treatment-related AEs were either mild or moderate. Thirty-three patients experienced serious AEs overall (initial phase: placebo 31.3%, 6 mg 26.1%; extension: placebo/6 mg 18.8%, 6 mg/6 mg 28.3%). Withdrawals occurred during the extension phase (placebo/6 mg 12.5%, 6 mg/6 mg 8.7%), but none were due to renal AEs. Laboratory parameters of renal functioning remained normal and there were no clinically-relevant renal AEs throughout the extension phase.
Conclusions: Ibandronate had a good safety and tolerability profile throughout the 4-year study, with no serious AEs caused by the treatment. The absence of treatment-related renal AEs and lack of laboratory abnormalities suggests that the renal safety profile of ibandronate is better than other intravenous bisphosphonates.

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Phase II trial of weekly paclitaxel (wP)+UFT for the treatment of patients with advanced breast cancer(ABC)

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Purpose: Phase II trials of combined chemotherapy for ABC using paclitaxel and 5-fluorouracil (Fu) have resulted in high response rates (50 to 60%) inspite of using as second line therapy following doxorubicin. Whereas wP has been reported for its effectiveness and usefullness, continuous administration of 5-Fu to maintain its plasma concentration (pc) needs hospitalization. We have already reported the effectiveness of addition of 5-Fu to wP, Phase I trial for wP+UFT orally, where the pc of 5-Fu is maintained by metabolic inhibition by uracil(ASCO 2002 Abs #1983). The recommended combination of wP+UFT for the treatment of patients with ABC is UFT 400 mg/body/day orally for 6weeks and P 80 mg/m^2 i.v. weekly for 6weeks of an 8-week cycle. A Phase II trial of wP+UFT for the treatment of patients with ABC is designed. The preliminary data of Phase II trial will be presented.
Methods: Patients with HER-2 negative, ABC without prior taxane in any setting were eligible. Patients were treated with or without Ps administered weekly for 6 weeks of an 8-week cycle. While the daily oral dose of UFT was fixed at 400 mg/body for 6 weeks, the dose of P was 80 mg/m^2 weekly as an hour infusion.
Results: A total of 21 patients were registered and randomized between 05/01 and 11/04, with 20 eligible for analysis(12 in wP+UFT, 8 in wP). The over all response rate(RR) is 65%. RR of wP+UFT and wP is 84.6% and 57.1% respectively. Ten patients were anthracycline pre-treated ABC. The most common reasons for discontinuation being progression/relapse (5%) and adverse events (5%). Grade 3 adverse events were 25%.
Conclusions: The combination of wP plus UFT is feasible alternative for the weekly paclitaxel therapy for advanced breast cancer.

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Gemcitabine (GEM) plus oxaliplatin (LOHP) as salvage treatment in anthracycline and taxane pretreated patients with advanced breast cancer (ABC)

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Background: To evaluate the efficacy and toxicity profile of GEM and LOHP in women with ABC pretreated with anthracyclines and taxanes.
Methods: Patients with histologically confirmed and measurable breast cancer, pretreated with anthracycline- and taxane-based chemotherapy for advanced disease, ECOG PS $\leqslant 2$, and adequate bone marrow, renal and liver function, were eligible. Patients received GEM 1500 mg/m^2 on day 1 and 8 and LOHP 130 mg/m^2 on day 8 every 3 weeks until progression or unacceptable toxicity. Toxicity was evaluated in each cycle and response every 3 cycles.
Results: Between 3/2001 and 6/2004, 31 patients were enrolled and all were evaluable for toxicity and response. The median age was 63 (range 46–72) years. Eight (26%) patients had received 1 and 23 (74%) 2 prior chemotherapy regimens. Bone metastases were present in 11 patients, liver mets in 11 pts, lung mets in 17 pts and lymph node mets in 10pts; 17 (55%) pts had $\geqslant 2$ metastatic sites. A total of 127 cycles were administered (median 3 cycles; range, 1–9). Grade 3–4 neutropenia occurred in 14 (45%) pts, thrombocytopenia in 6 (19%) pts, and asthenia in 4 (13%) pts. CR was achieved in 1 (3%) and PR in 4 (13%) patients (ORR = 16%;