progression-free survival of nab-paclitaxel 150 mg/m^2 weekly, a phase III trial comparing this dose to docetaxel 100 mg/m^2 every 3 weeks is planned.

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Bone metastases factors in an early breast cancer

B. Madej-Czerwonka[1], J. Szumilo[2], F. Burdan[3], A. Chroscicki[4], R. Maciejewski[3]. *[1]District Hospital of Lublin, Surgical Oncology Department, Lublin, Poland; [2]Medical University of Lublin, Clinical Pathomorphology Department, Lublin, Poland; [3]Medical University of Lublin, Anatomy Department, Lublin, Poland; [4]District Hospital of Lublin, General Surgery Department, Lublin, Poland*

Formation of distant metastases that affect the skeletal system is the main cause of failure in the treatment of the early breast cancer. Presently applied prognostic factors do not sufficiently determine the risk of systemic dissemination.

The aim of the study was to evaluate selected neoplastic factors in reference to the formation of bone metastases in patients with early breast cancer.

Methods: 164 patients were operated and monitored post-operatively for five years. The tumour size and grade, lymph nodes involvement, expression of estrogen (ER), progesteron (PgR) and HER-2 receptors; level of cancer antigen 15−3 (CA15−3), Ki-67, Bcl-2, Bax, Bax/Bcl-2, Fas-L, TNF, ICAM-1, sICAM-1 were analyzed. Blood samples were collected pre-operatively. The expression of Ki-67, Bcl-2, Bax, Fas-L, TNF-α, ICAM-1, ER, PgR, HER-2 was determined immunohistochemically in primary tumour. The level of the serum marker was measured using ELISA. The prognostic value of the investigated factors was determined on the basis of clinical data.

Results: The overexpression of Ki-67, Bax, Fas-L, TNF, a low expression of Bcl-2 and ICAM-1, increased Bax/Bcl-2 ratio, increased level of sICAM-1 and CA 15-3, as well as higher number of involved axillary lymph nodes are characteristic for systemic dissemination. The analysis of 5-year survival time has revealed a higher number of deaths among patients with low expression of Bcl-2.

Conclusions: The overexpression of Bax and the increased level of sICAM-1 determines the formation of bone metastases in patients with an early breast cancer. On the basis of multifactorial analysis it may be concluded that the following positive factors in the prognosis for 5-year survival time are observed at the same time: low expression of Ki-67, overexpression of Bcl-2, low expression of Bax, as well as decreased Bax/Bcl-2 ratio.

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Trastuzumab plus intravenous or oral vinorelbine in chemonaive patients with HER-2 overexpressing metastatic breast cancer – final results of an extended phase II trial

G. Bernardo[1], R. Palumbo[1], A. Bernardo[1], C. Teragni[1], G. Poggi[1], A. Delmonte[1], A. Amatu[1], M. Frascaroli[2], I. Jedrychowska[2], M. Strada[2]. *[1]Fondazione Maugeri, Medical Oncology II, Pavia, Italy; [2]Fondazione Maugeri, Rehabilitative Oncology, Pavia, Italy*

Background: The activity of trastuzumab (T) combined with chemotherapy in HER2-overespressing (HER2+) BC has been well documented in randomized trials, in both the adjuvant and metastatic setting. We report the updated results of our expanded experience on a combined regimen of T and Vinorelbine (VNR) given intravenously or orally as first-line treatment in HER2+ metastatic BC patients (pts).

Patients and methods: A total of 83 consecutive pts with histologically confirmed, measurable MBC, tumors scored as +3 positive for HER2 by immuno-histochemistry or FISH+, no prior chemotherapy for the metastatic disease were enrolled. Median age was 53 years (range 31–70); prior adjuvant chemotherapy in 63%; prior hormonal in 45%; visceral metastases in most cases (liver 56%, lung 34%). In the first 58 patients (Group A) treatment consisted of i.v. T (4 mg/Kg loading dose as a 90'infusion, then 2 mg/kg weekly in 60') followed by i.v. VNR (25 mg/m^2 weekly as 10' infusion) without a break, with one cycle consisting of 4 consecutive weeks. In the following 25 patients (Group B) VNR was given orally at the dose of 60 mg/m^2 weekly.

Results: All pts received at least 3 courses of therapy (median 5 and 4 per patient, respectively, range 3−12). The worst toxicity was haematological in both groups (grade 4 leukopenia in 11% and 10% of pts, respectively) with no significant cardiac or neurologic side effects. The overall response rate (RR) was 86% in Group A (95% CI 75%-92%), with 6 complete and 44 partial remissions, and 84% in group B (95% CI 63%-93%), with 4 complete and 17 partial remissions. Median TTP was 12 months (range 6−19); median overall survival was 34 and 31 months, respectively.

Conclusions: Our results confirm the high antitumoral activity of T/VNR combination as first-line treatment in HER2+ metastatic BC pts, with acceptable toxicity and no significant difference in patient compliance between the intravenous and oral VNR formulation, further improving the possibility of a "personalized" therapeutic strategy, based on the different clinical situations and patient preferences.

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A single-institution experience from the Lapatinib Expanded Access Program – effect of lapatinib and capecitabine combination therapy on CNS metastases in patients with ErbB2+ metastatic breast cancer

B. Kaufman[1], R. Weitzen[1], A. Goldfarb[1], N. Ephrat[2], I. Kuchuk[1], T. Golan[1], I. Wolf[1], R. Elia[1]. *[1]The Chaim Sheba Medical Center, Oncology, Ramat Gan, Israel; [2]Kaplan Medical Center, Oncology, Rehovot, Israel*

Background: Brain metastases affect 25% to 30% of women with ErbB2+ metastatic breast cancer (MBC) and are associated with a high burden of disease and a poor prognosis. Cranial radiotherapy is effective as initial therapy for brain metastases; however, there is no standard treatment for patients whose CNS disease then progresses. Lapatinib is an oral, small molecule, tyrosine kinase inhibitor of ErbB1 (EGFR) and ErbB2 (HER2). When combined with capecitabine, lapatinib significantly improves time to disease progression in patients with ErbB2+ MBC previously treated with anthracyclines, taxanes, and trastuzumab (ATT). The Lapatinib Expanded Access Program (LEAP) was designed to provide access to lapatinib plus capecitabine before the commercial availability of lapatinib for the treatment of patients who have progressive disease (including CNS metastases) after ATT.

Material and Methods: Patients enrolled in LEAP were treated with lapatinib 1,250 mg/day and capecitabine 1,000 mg/m^2 PO BID. Among patients with CNS disease progression before study entry, response (RECIST) was assessed on-study via CT or MRI at baseline and every 6 weeks. Neurological symptoms were assessed via clinical assessment.

Results: Eleven of 48 (23%) patients (aged 37 to 62 years) enrolled at this single institution had a history of CNS disease; each of these 11 patients had received whole-brain radiotherapy (300 cGy $\times$ 10 fractions) before study entry, and 2 patients had also undergone surgical resection of brain lesions. Patients initially presented with various neurological symptoms including severe headache, loss of balance and gait disturbances, dizziness, difficulty in focusing visually, and vomiting. Among 7 patients evaluable for CNS response, 2 patients had a complete response, 2 patients had a partial response, and 3 patients had stable disease after treatment with lapatinib plus capecitabine. Marked neurological improvement was observed in 4 patients, and mild improvement in 2 patients. Lapatinib plus capecitabine was well tolerated; as expected, rash, diarrhea, and hand foot syndrome were the most common toxicities.

Conclusions: These preliminary results support previous hypothesis-generating data that lapatinib plus capecitabine is active in patients with ErbB2+ MBC and brain metastases previously treated with trastuzumab and cranial irradiation. Further investigation of lapatinib plus capecitabine in patients with ErbB2+ CNS metastases is warranted.

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A phase II study of gemcitabine plus capecitabine (GC) in heavily pre-treated metastatic breast cancer patients. The Swedish GC Breast Cancer Study Group

A. Malmström[1], J. Hansen[2], L. Malmberg[3], L. Carlsson[4], J.H. Svensson[5], J. Ahlgren[6], C. Ahlin[7], T. Jansson[8], R. Westberg[9]. *[1]Dept of Oncology, Linkoping, Sweden; [2]Dept of Oncology, Karlstad, Sweden; [3]Dept of Oncology, Jönköping, Sweden; [4]Dept of Oncology, Sundsvall, Sweden; [5]Dept of Oncology, Göteborg, Sweden; [6]Dept of Oncology, Gävle, Sweden; [7]Dept of Oncology, Örebro, Sweden; [8]Dept of Oncology, Trondhein, Norway; [9]Dept of Oncology, Stockholm, Sweden*

Background: The gemcitabine, capecitabine (GC) combination is reported to be effective and tolerable in advanced pancreatic cancer. The aim of this study was to explore the value of GC in heavily pre-treated metastatic breast cancer pts.

Material and Methods: At inclusion, all pts had failed anthracyclines and taxanes and if applicable also endocrine treatment. At study entry 41% of pts presented with more than 2 metastatic sites with bone (68%) and liver (62%) beeing the most prominent. Gemcitabine (1250 mg/m^2, d1+8) and capecitabine (800 mg/m^2 twice daily, d1–14) were administered according to a 3-week schedule. GC was given as 3rd line (18 pts) or 4th line (14 pts) or 5th line (2 pts) chemotherapy. Lab tests were done on day 1+8 in cycles. Subjective toxicity was recorded according to the NCI-CTC v.2.0 criteria. Tumour evaluations were done every 3rd months according to the RECIST criteria. The primary objective was to investigate time to