assessed the risk of brain metastases in a large unselected series of HER2-positive MBC patients.

Material and Method: Study group included 173 consecutive HER2-positive (immunohistochemistry 3+ or FISH+) MBC patients from five Polish institutions. Patient age ranged from 30 to 81 years (median 49 years); 83 patients were premenopausal (47.9%), 88 – postmenopausal (50.9%) and in 2 patients menopausal status was unknown (1.2%). Dominant site of disease included viscera in 130 (75.1%), soft tissue in 21 (12.1%), bones in 19 (11.0%) and was unknown in 3 patients (1.7%). Data on ER/PR status were available for 151 patients (87.3%). ER+/PgR+, ER+/PgR-, ER-/PgR+, ER-/PgR- phenotypes were represented by 19.9%, 13.9%, 4.0% and 62.3% of this group, respectively. 66 patients (38.2%) had received prior (neo)adjuvant chemotherapy, 11 (6.4%) – adjuvant hormonotherapy, and 53 patients (30.6%) – a combination thereof. Disease-free interval to the development of MBC ranged between 0 and 124 months (median 14 months). A total of 126 patients (72.8%) received trastuzumab for MBC, usually in combination with chemo- and/or endocrine therapy. Statistical analysis included contingency tables, chi-square test, Kaplan-Meier survival analysis and Cox proportional hazard model.

Results: Median follow-up from the development of MBC was 3.8 years (range 0.5–12.3 years). 45 patients (26.0%) developed brain metastases including 26.2% and 25.5% who did and did not receive trastuzumab ($p = 0.93$). Median time to brain relapse from the diagnosis of MBC was 10 months (range, 0 to 65 months). Detailed analysis of factors related to the risk of CNS metastases will be presented during the conference.

Conclusion: HER2-positive MBC patients carry increased risk of brain relapse which does not seem to be reduced with trastuzumab treatment. This calls for more effective preventive measures.

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Oral bisphosphonates are associated with low persistence and compliance (adherence) in patients with breast cancer

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Introduction: It has been shown that skeletal complications can be reduced by bisphosphonates in patients with bone metastases. Because the optimum clinical benefit is only achieved in patients who remain on therapy, we studied the persistence and compliance (adherence) with oral bisphosphonates in patients with breast cancer in a naturalistic setting.

Material and Methods: Persistence and compliance with oral bisphosphonates for breast cancer patients was analysed using claims data from a large German sickness fund covering the time period from January 2000 to December 2003. Patients were included if they had an ICD-10 diagnosis for breast cancer AND were receiving oral bisphosphonates. The minimum time of continuous enrollment after the first observed oral bisphosphonate prescription was 7 months. Persistence was defined as the duration of continuous prescription refill without an interruption of longer than 30 days. Compliance (adherence) was measured in terms of the medication possession ratio (MPR: dispensed medication supply in a given period of time).

Results: There were n = 231 patients fulfilling the inclusion criteria with a mean age of 63.2 years (37–92 years). From these patients 102 (44.2%) received clodronate as the first prescription followed by 69 (29.9%) with alendronate, 31 (13.4%) with risedronate, and 29 (12.6%) with etidronate. A bone metastasis diagnoses was recorded for 58 patients (25.1%). At the end of 6 months, only 37.7% of the patients were found to be persistent with their oral bisphosphonate therapy. The median therapy duration was 103 days. A good compliance was assumed if an MPR of at least 80% was found. According to this definition, no more than 36.8% of the breast cancer patients showed a good compliance within 180 days following the first detected bisphosphonate prescription.

Conclusions: We found only 37.7% of breast cancer patients still remaining on bisphosphonate therapy after six months. It has been shown that an effect on skeletal morbidity outcomes cannot be expected before oral bisphosphonates have been administered for at least six months (Ross et al., Health Technol Assess 2004; 8(4):1–176). Therefore, further study needs to be evaluated to determine the impact of compliance and persistence on the outcome of skeletal morbidity such as severe bone pain, pathologic fracture, spinal cord compression, and hypercalcemia of malignancy.

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Intravenous and oral ibandronate have better safety and tolerability profiles than zoledronic acid: evidence from comparative phase III trials

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Recommendations state that all breast cancer patients with bone metastases should be treated with a bisphosphonate. Ibandronate is a single-nitrogen, non-cyclic bisphosphonate available in intravenous and oral formulations that had safety profiles comparable to placebo in phase III trials. Here, safety data from two comparative, open-label, phase III trials are reported. Patients were randomized to receive ibandronate or zoledronic acid for 12 weeks. In trial A, ibandronate-treated patients received intravenous ibandronate 6 mg on Day 1 (15-minute infusion) then daily oral ibandronate 50 mg from Day 2 onwards. In trial B, ibandronate-treated patients received daily oral ibandronate 50 mg only. The comparative treatment in both trials was intravenous zoledronic acid 4 mg (15-minute infusion) every 3–4 weeks. Trial A recruited 77 patients with either breast cancer or multiple myeloma and ⩾1 confirmed bone lesion; trial B recruited 274 metastatic breast cancer patients. All adverse events (AEs) were recorded. Results showed that fewer patients experienced AEs with intravenous or oral ibandronate than with zoledronic acid (trial A: 64% vs 74%; trial B: 65% vs 76%). In particular, the incidence of AEs on Days 1–3 was lower for ibandronate than zoledronic acid (trial A: 26% vs 47%; trial B: 8% vs 47%). This was mainly because of a zoledronic acid-associated acute-phase response (APR); pyrexia or flu-like symptoms occurred in 13% of the ibandronate group compared with 26% of the zoledronic acid group in trial A, and 1% compared with 27% in trial B. In both studies, fewer patients reported bone pain as an AE with ibandronate than zoledronic acid (trial A: 8% vs 16%; trial B: 12% vs 21%). The incidence of gastrointestinal (GI) AEs was slightly higher for ibandronate than zoledronic acid (trial A: 23% vs 21%; trial B: 23% vs 18%). Serious AEs and withdrawal rates were similar between treatment groups. In these comparative studies, fewer patients experienced AEs with ibandronate than zoledronic acid, regardless of ibandronate formulation or dosing schedule. In particular, there was a lower incidence of APR AEs for ibandronate than zoledronic acid, even with intravenous ibandronate treatment. Ibandronate is a well-tolerated treatment for metastatic bone disease with apparent AE advantages over intravenous zoledronic acid and no renal safety issues.

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Does Her2 status change in metastases of breast carcinomas?

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Introduction and Aim: There has been an ongoing debate as to whether metastatic breast carcinoma may change its Her2 status or it remains similar to that of the primary tumor. Our aim was to investigate various metastatic sites from the point of view of Her2 expression and to compare the Her2 status of the metastasis to that of the original primary tumor, where available.

Patients and Methods: Thirty six metastasis from primary breast carcinomas were investigated. Liver, pleura, bone marrow, skin, brain, urinary bladder metastases were collected. 11 cytological, 9 biopsy and 14 excision specimens, and, 2 metastases found at autopsy were available for this study. In 20 cases the Her2 status of the primary tumor was also known. The Her2 status of the primary tumor was known a) from the original histology report, b) was repeated during this study both by immunohistochemistry and FISH. The metastases were investigated both by immunohistochemistry and FISH. For immunohistochemistry, the ready to use CB11 (Novocastra) antibody was applied. FISH was performed using the the Ventana Benchmark system.

Results: Altogether, 22% (8/36) of the metastatic tumors proved to be Her2 positive by FISH. In the 20 cases where both the primary and the metastatic tumors were available for the study, 25% (5/20) of the primary tumors and 20% (4/20) of the metastatic tumors showed Her2 gene amplification by FISH. The liver metastasis of the fifth Her2 positive primary tumor was diagnosed by FNAB, and the Her2 status of this metastasis was established by immunocytochemistry with a result of score 3+. In case-by-case comparison, FISH positive cases had FISH positive metastases. However, slight changes in immunohistochemical results could be detected: from score 0 to 1+, 1+ to 2+, 2+ to 3+ occurred in single cases. There were three cases showing slight changes in the opposite direction: from 3+ to 2+