toxicities were: neutropenic infection that was 16.8% vs 9.2% respectively for TH and TCH, thrombocytopenia (2% vs 15%), asthenia (5% vs 12%), anemia (5% vs 11%), and diarrhea (2% vs 10%). Two pts died (1.5%) due to sepsis in TCH. Absolute LVEF decline >15% were seen in 5.5% vs 6.7% of pts. One pt (0.8%) had a symptomatic CHF in TH arm. The serum HER2 ECD analysis is underway and will be presented.
Conclusion: Both TH (T 100) and TCH (T 75) were highly effective treatment regimens in women having HER2-positive MBC, demonstrating high response rates, median TTP >10 months, and median overall survival >36 months in both TH and TCH. Cardiac toxicity was no significant problem with either treatment.

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Multiple lines of trastuzumab provide a survival benefit for women with metastatic breast cancer: results from the Hermine cohort study

E.C. Antoine[1], J.M. Extra[2], A. Vincent-Salomon[3], L. Bergougnoux L[4], F. Campana[4], M. Namer[5]. *[1]Clinique Hartmann, Oncology, Neuilly sur Seine, France; [2]Institut Paoli Calmettes, Oncology, Marseille, France; [3]Institut Curie, Oncology, Paris, France; [4]Roche, Oncology, Neuilly-sur-Seine, France; [5]Centre Azuréen de Cancérologie, Oncology, Nice, France*

Background: The efficacy and safety of trastuzumab (Herceptin®; H) in combination with taxanes have been demonstrated in clinical trials of patients (pts) with HER2-positive metastatic breast cancer (MBC). There is considerable interest in the efficacy of continuing H after disease progression. Data from the Hermine cohort study of H for MBC in routine clinical practice were analysed to determine whether continuation of H is beneficial.
Material and Methods: Hermine was an observational French cohort study of pts with HER2-positive MBC who began their initial H treatment between January and December 2002. Study end points included duration of treatment, progression-free survival (PFS) and overall survival (OS). Minimum follow-up was 2 years. We present data from exploratory analyses of pts treated with H in the first- or second-line setting who continued to receive H-based treatment at disease progression or who discontinued.
Results: A total of 623 pts were enrolled, of whom 221 and 117 received their first H regimen as first- or second-line treatment, respectively. Among pts receiving first-line H, median OS from first H treatment was longer in pts who continued to receive H compared with those who discontinued (not yet reached after 27.8 months' follow-up vs 16.8 months [95% CI: 12.5−19.5]; $p < 0.0001$). Similarly, in the first-line setting, OS at 2 years was 73.7% in pts who continued H compared with 24.7% in pts who discontinued. Median OS from the date of first progression for pts who received first-line H was 21.3 vs 4.6 months for pts who continued H compared with those who discontinued, respectively ($p < 0.0001$). Among pts receiving second-line H, median OS from the first H treatment was again longer in those who continued treatment with H after progression compared with those who discontinued (27.2 vs 15.6 months, respectively; $p = 0.076$). In addition, median OS from the date of first progression for pts who received second-line H was 15.5 vs 11 months for pts who continued H compared with those who discontinued H, respectively ($p = 0.023$).
Conclusion: Continuing H after disease progression in women with HER2-positive MBC who received H in the first- or second-line setting appears to be associated with a survival advantage.

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Prediction of brain relapse (BR) in HER-2 positive metastatic breast cancer (MBC) patients (pts)

R. Duchnowska[1], B. Czartoryska-Arlukowicz[2], B. Radecka[3], B. Szostakiewicz[4], K. Sosinska[4], A. Karpinska[5], R. Dziadziuszko[4], E. Staroslawska[6], T. Kubiatowski[6], C. Sczylik[1]. *[1]Military Institute of Medicine, Oncology, Warsaw, Poland; [2]Regional Cancer Center, Oncology, Bialystok, Poland; [3]Regional Cancer Center, Oncology, Opole, Poland; [4]Medical University, Oncology and Radiotherapy, Gdansk, Poland; [5]Regional Oncology Center, Oncology, Szczecin, Poland; [6]Regional Oncology Center, Oncology, Lublin, Poland*

Background: We have earlier demonstrated a high risk of BR in HER2 positive MBC pts (J Clin Oncol, 2006; 24, 18S). The present study, based on longer follow-up and increased number of events, includes extensive analysis of clinical and pathological factors determining the risk of BR in this group.
Material and Methods: Study group included 264 consecutive HER2-MBC pts aged from 24 to 77 years (median 49 years). A total of 131 pts (50%) were premenopausal, 130 (49%) – postmenopausal and 3 (2%) – with unknown menopausal status. Dominant site of disease included soft tissue (28 pts, 11%), bones (26 pts, 10%) and viscera (210 pts, 80%). A total of 210 pts (80%) were administered trastuzumab for metastatic disease, usually in combination with other systemic therapies. Statistical analysis included contingency tables, chi-square test, Kaplan-Meier survival analysis and Cox proportional hazard model.
Results: After a median follow-up of 2.8 years the clinical BR occurred in 75 pts (28%). Median time from treatment dissemination to BR was 10 months (range, 0−81 months), and the cumulative one- and two-year risk of BR was 17% and 31%, respectively. The cumulative one-year risk of BR in post- and premenopausal pts was 8% and 24%, and the two-year risk – 29% and 33%, respectively ($p = 0.019$). The cumulative one- and two-year risk of BR in pts administered trastuzumab was 11% and 25%, respectively, compared to 14% and 33%, respectively in pts who did not receive trastuzumab ($p = 0.54$). In the multivariate analysis premenopausal status (HR = 1.96; $p = 0.008$), and time to distant relapse shorter than two years (HR = 1.72; $p = 0.031$) were significantly related to the risk of BR, whereas lobular carcinoma was at borderline level (HR = 2.12, $p = 0.061$). Based on the multivariate analysis a prognostic index of the risk of BR in HER-2 positive MBC pts was developed. In the low-risk group (0−1 unfavorable variables; 68% of all pts) the cumulative one- and two-year risk of BR was 11% and 23%, respectively, compared to 28% an 46%, respectively in the high-risk group (2−3 unfavorable variables; 32% of all pts). The hazard risk of BR in the high- vs. low-risk group was 2.42 ($p < 0.001$). The median survival in pts with BR was 9 months, with 39% and 13% one- and two-year survival probability, respectively.
Conclusions: Clinical and pathological factors may select MBC patient categories with particularly high risk of BR in whom preventive strategies should be considered.

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Phase III study of ixabepilone plus capecitabine in patients with metastatic breast cancer (MBC) progressing after anthracyclines and taxanes: subgroup analysis of patients receiving ixabepilone in the first-line setting

J. Jassem[1], E. Thomas[2], H. Gomez[3], R.K. Li[4], H.C. Chung[5], L.E. Fein[6], V.F. Chan[7], R.A. Peck[8], P. Mukhopadhyay[8], H. Roché[9]. *[1]Medical University of Gdansk, Department of Oncology and Radiotherapy, Gdansk, Poland; [2]Kaiser Permanente, Oncology, Oakland, USA; [3]The Instituto Nacional de Enfermedades Neoplasicas, Oncology, Lima, Peru; [4]The St. Luke's Medical Center, Oncology, Quezon City, Philippines; [5]The Yonsei Cancer Center, Oncology, Seoul, Korea; [6]The Centro de Oncologia Rosario, Oncology, Sante Fe, Argentina; [7]The Veterans Memorial Medical Center, Oncology, Quezon City, Korea; [8]Bristol-Myers Squibb Research and Development, Oncology, Wallingford, USA; [9]The Institut Claudius Regaud, Oncology, Toulouse, France*

Background: Anthracyclines and taxanes are increasingly used as adjuvant therapy in breast cancer. Patients who progress within 1 year of adjuvant taxane and anthracycline therapy have limited therapeutic options for first-line treatment in the metastatic setting. Ixabepilone, a semi-synthetic analog of epothilone B, was developed to overcome tumor resistance mechanisms. This phase-III trial evaluated ixabepilone plus capecitabine vs capecitabine alone.
Methods: 752 MBC patients resistant to anthracyclines and taxanes were randomized to ixabepilone (40 mg/m^2 iv over 3h on day 1 every 3 weeks) in combination with capecitabine (2000 mg/m^2 po in 2 divided doses, on days 1−14 of a 21-day cycle), or capecitabine alone (2500 mg/m^2 on the same schedule). Resistance was defined as disease progression within 3−4 months following anthracycline/taxane in the metastatic setting and 6−12 months following adjuvant anthracycline/taxane therapy. A prospectively-defined subset analysis was performed in patients who received ixabepilone plus capecitabine as first-line treatment after adjuvant anthracycline/taxane.

	Total population		First-line after adjuvant A/T[a]	
	Ixabepilone + capecitabine (N = 375)	Capecitabine (N = 377)	Ixabepilone + capecitabine (N = 25)	Capecitabine (N = 30)
PFS (mo), median (95% CI)	5.8 (5.5–7.0)	4.2 (3.8–4.5)	7.0 (4.5–8.8)	2.1 (1.4–4.2)
Hazard ratio (95.17% CI)	0.75 (0.64–0.88)		0.46 (0.25–0.85)	
Objective response rate (%)	35	14	44	10

A/T, anthracycline/taxane.

Results: Ixabepilone plus capecitabine was superior to capecitabine with a 40% prolongation of median progression-free survival (PFS) ($p < 0.001$). Fifty-five patients received ixabepilone plus capecitabine or capecitabine as first-line therapy. PFS was again prolonged for patients receiving