trastuzumab to chemotherapy (CT) significantly improves survival in early and advanced breast cancer. The purpose of this retrospective study was to explore the pattern of outcome in a cohort of MBC patients treated with T-based chemotherapy in a single institution. T was approved in Europe in 2000 and in 2001 all pts had access to T according HER2+ status.

Methods: Women with de novo or recurrent breast cancer treated with trastuzumab at Institut Curie between 2001 and 2006 with HER2+ status (IHC 3+ or FISH +) were identified from the Institut Curie database. Disease was classified in two groups: patients who received T upfront and those who received T after one or several CT regimens. Overall survival (OS) was defined as the time from the date of the first metastasis to the date of death or last follow-up and was estimated using the Kaplan-Meier product method.

Results: The final analysis included 244 patients. Median age was 53.4 yrs (29−80). Median time from primary and first metastasis was 22 mths (0–238). Visceral metastasis were present in 153 pts (63%) and 125 pts (51%) presented multiple sites. One hundred pts (42%) developed brain metastasis during the course of disease. One hundred and sixty five pts (68%) received T as first line, 79 pts (32%) after a median of one line of CT (median 1, range 1−5). One hundred and twenty four pts (52%) received more than 3 regimens. The median overall survival was 53 mths (4–113), similar in both groups. However there is a major bias: pts with very aggressive disease not treated upfront with T not have not been offered delayed T and don't appear in the analyzed population. Patients who developed brain metastasis had a median survival of 41 mths (11−90). Complete characteristics of pts will be presented.

Conclusions: The introduction of T has altered the natural history of HER2+disease. Even outside a clinical trial, our results show that the addition of T to CT improves the prognosis of MBC patients with HER2+ disease. Prolongation of T after progression with other CT appears beneficial, even in pts with a high disease burden. The high incidence of brain metastases remains an issue in such a population and new strategies of prevention and treatment need to be addressed.

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Affecting factors to the survival of breast cancer with brain metastasis

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Background: Brain metastasis (BM) associated with breast carcinoma commonly occur in later stage of metastatic disease and strongly affect survival of the patient. Recently, several studies reported that breast cancer subtypes may be related with central nervous system recurrence rate and survival after BM. Aim of this study was to identify tumor characteristics and the affecting factors to the survival of breast cancer patients with BM at our oncology hospital.

Material and Methods: Medical records of 123 primary breast cancer patients with brain metastasis receiving treatment in a cancer center between january 2004 to August 2009 were rewieved retrospectively. 105 patients whose steroid hormon receptors (estrogen receptor (ER) and progesteron receptor (PgR) and HER-2 status of their tumors were assesed hve been included in the study.

Results: Median age at the diagnosis of breast cancer was 42 (range 24−78 years). Except one male patient, all of the patients were women. Only seven patients had metastatic disease at the presentation. Sixty (57.1%) patients had HER-2 positive tumors. Thirteen (12.4%) patients had triple negative tumors. Sixtyeight (64.7%) patients had ER and/or PgR positive tumors. BM was the first site of relaps in 16 (15.2%) patients. Sixtyfive (61.9%) patients had multiple BM, 10 (9.5%) had both metastasis of brain parenchyma and the leptomeninges. Seventeen (16.2%) patients underwent brain surgery or cyber- or gamma-knife surgery for BM. Ninetythree (90.3%) patients received whole-brain radiotherapy. No HER-2 positive patients received adjuvant trastuzumab therapy. Fortyfour patients was given trastuzumab for treatment of metastatic disease.

Median disease free survival (DFS) was 18.3 months (range 0–183 months). Median overall survival was 35.1 months (range 1–208). Median survival after BM was 6.2 months (range 0−50 months). Median survival of four groups of patients after BM were as follows respectively:

for triple negative group was 5.47 months (range 0−26 months);
for ER and/or PR positive and HER-2 negative group was 9.6 months (range 0−50 months);
for ER and/or PgR positive and HER-2 positive group was 8.2 months (range 0−23 months);
for ER and/or PgR negative and HER-2 positive group was 7.1 months (0−18 months).

Multiple linear regression (backward) model showed that having young age (r: −1.93; CI%95: −0.375–0.001); p = 0.056), ER positivity (r: 2.34; CI%95: 0.62−7.5; p = 0.021) and adjuvant chemotherapy (r: 1.68; CI%95: −0.06–7.4; p = 0.09) affected the survival positively. Patients treated with cranial RT had longer survival with BM (4.9±5.07 vs. 9.9±9.3 months) but the difference was marginally significant (p = 0.09).

Conclusion: Survival after BM of the patients with triple negative and HER-2 positive breast cancer are shorter than steroid hormon receptor positive and HER-2 negative breast cancer with BM. New effective treatment strategies are required for these poor risk groups.

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Chemotherapy and bevacizumab combinations in second-line or more for metastatic breast cancer: efficacy and toxicity results

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Background: In first line metastatic breast cancer (MBC), bevacizumab (B) in combination with chemotherapy [taxanes (T), anthracyclines or capecitabine (C)] is more efficient in comparison with the same mono chemotherapies regimens. However, such combinations are not approved in subsequent lines of therapy even if the patients were treated in first line MBC without B before the BT combination approval. in order to evaluate the efficacy and toxicity profile of these combinations in at least second lines of treatments for MBC we have extract from our chemotherapy database the population of patients treated with bevacizumab-chemotherapy combinations for MBC.

Methods: A retrospective analyzis was performed on all the MBC patients treated with B combined with chemo, between 1/2007 and 12/2008, in the oncology departments of APHP Tenon hospital in Paris. Statistics were descriptive for the population, the efficacy and the toxicity.

Results: 55 patients received B combined with T in 34 cases (62%) or C/5FU in 16 cases (29%). Median age was 57.3 years [37.7–76.8]; 55.2 years [37.7–76.8] in the B-T treated group and 60.9 years [48.5–76.8] in the B-C/5FU treated group. Median number of previous lines was 4 [2−11]. At a median follow up of 11 months [0−28] 65% of all the patients are still alive. According to the presciber evaluation the median duration of the clinical benefit, measured as the delay between the first day of B-chemo combination and the date of progression or last news date, was of 4.2 months [0.7–16.6]; 4.2 months [0.7–16.6] in the B-T treated group and 5 months [0.7−8.3] in the B-C/5FU treated group. 27 patients (49%) had an objective response and 13 (24%) had no clinical benefit and readily progressed under therapy. We didn't find predictive factor for clinical benefit of the combination but we didn't find that previous taxane therapy for MBC was associated with a worst efficacy of B-chemotherapy regimens. Considering the toxicity profile, we didn't find different outcomes comparing to the reported results in the randomized phase III trials concerning the first line MBC treatments with chemotherapy and B.

Conclusions: in this retrospective analysis, in heavily pretreated MBC patients the combination of B-chemotherapy seems feasible without an increasing level of toxicity. However, this strategy had to be evaluated in a porspective trial considering the absence of approval of B-chemotherapy combinations beyond 1st line MBC treatment.

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Prognostic factors to predict outcomes in patients with HER2-overexpressing metastatic breast cancer treated with trastuzumab containing chemotherapy as first or second line therapy: prognosis grouping according to the prognostic factors

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Background: To investigate prognostic factors to influence overall survival (T-OS) in patients with HER2 overexpressig metastatic breast cancer (HO-MBC) who underwent first or second line trastuzumab containing chemotherapy.

Patients and Methods: From January 2003 to May 2008, clinical and laboratory findings of 89 patients at the time of trastuzumab administration were analyzed to correlate with T-OS.

Results: In univariate analysis, estrogen and progesterone receptor positivity (p = 0.047), lung metastasis (p = 0.006), liver metastasis (p = 0.006), 3 or more metastatic sites (p = 0.002), elevated aspartate aminotrasferase (AST) (p = 0.005), elevated alkaline phosphatase (0.039), and elevated total bilirubin (p = 0.001) were significant factors to affect T-OS. In multivariate analysis, presence of lung metastasis (p = 0.004, hazard ratio=5.440, 95% CI = 1.722–17.180) and elevated AST (p = 0.004, hazard ratio=4.035, 95% CI = 1.549–10.514) were significant poor risk factors for T-OS. Based on risk factors in multivariate analysis, three prognosis groups were categorized: good prognosis group (risk factor = 0),

28 patients (32%); intermediate (risk factor=1), 50 patients (56%); poor (risk factor=2), 11 patients (12%). Median T-OS of good, intermediate and poor prognosis group was not-reached (more than 59.7), 29.7 and 15.3 months, respectively ($p < 0.001$).

Conclusion: Prognosis grouping based upon the prognostic factors might be useful to predict outcomes of patients with HO-MBC treated with trastuzumab containing chemotherapy.

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Phase II study of S-1 in combination with irinotecan (CPT-11) for patients with advanced/recurrent breast cancer (KSCOG-BC01)

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Background: Irinotecan and S-1 have been shown to be effective in patients with advanced/recurrent breast cancer and they have a considerable single-agent activity, respectively. We evaluated the combination of irinotecan (CPT-11) and S-1 as first-line chemotherapy for advanced or recurrent breast cancer (BC).

Methods: All patients with histologically confirmed BC with unresectable or metastatic diseases, measurable lesions, PS 0−2, age between 18 and 80, and no contraindication to chemotherapy were eligible in this study. Prior adjuvant chemotherapy finished at least 6 months before enrollment was allowed. Treatment included S-1 80 mg/m^2 p.o. twice daily on days 3 to 7, 10 to 14, and 17 to 21 and CPT-11 60 mg/m^2 i.v. on day 1, 8, 15 with a 1-week interval until disease progression or unacceptable toxicities. Both recommended doses of S-1 and CPT-11 was based on our previous Phase I study.

Results: Between May 2007 and August 2009, total 16 pts were enrolled in this study. The median age was 56.5 years (range, 38−73). Nine pts had recurrent disease after previous curative mastectomy and 7 had previous adjuvant chemotherapy. After a median 3 (range, 1−9) cycles of chemotherapy, 16 pts were evaluable for toxicity and 9 pts for response. The overall response rate was 33.3%, including 0 CR, 3 PRs, 4 SDs, and 2 PDs. The clinical benefit rate was 77.8%. Commonly observed grade 3/4 adverse events were neutropenia (12.5% of patients), diarrhea (12.5%). There was no neutropenic fever or treatment-related death.

Conclusions: The combination of CPT-11 and S-1 appear to have well efficacy, manageable toxicity and is well tolerated in patients with advanced/recurrent BC. Further studies of this combination are still ongoing.

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Clinical and pathological prognostic characteristic of breast cancer patients with brain metastases

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Improvement in breast cancer patient's treatment leads to life prolongation. This is connected with rising incidence of brain metastases (BM) which occurs in up to one third of patients with metastatic breast cancer. The aim of this study is to analyze clinical and pathological factors in patients with BM. This is a retrospective review of 177 breast cancer patients treated with brain radiotherapy between 2005–2007 at two Cancer Centers in Gliwice and Krakow.

Patient's age at the time of diagnosis was 50 years (28−80). Patient's stages at the time of cancer diagnosis were: T_{1-2} 42% T_{3-4} 37%, N_{0-1} 56%, N_{2-3} 23%. Majority were treated with radical intent 81%, 19% were treated palliatively. 79% were treated with chemotherapy, 36% with hormonal therapy, 44% of patients underwent loco-regional radiotherapy treatment. Pathological reports showed that lymph nodes metastases were not present only in 28%. Tumours were ER, PR receptor positive only in 34% and 26%, and only in 10% for ER and 12% for PR were highly positive. In 36% HER2 was negative, high expression or amplification was in 36%. All brain metastases were treated with radiotherapy, 20% metastasectomy, 25% stereotactic irradiation, in combination with WBRT 19% or alone 6%.

Median time from diagnosis to BM was 2.74 years (range 0−19). Single BM were in 29%, multiple metastases in 30%, remaining had 2−7 lesions. First metastatic site was brain in 41%. Median time from treatment dissemination to brain relapse was 0.1 years (range 0−9.2). In patients treated with radical intent, median time to BM was longer in ER+ 4.5 years vs ER− 2.9. ($p = 0.1$) and in PR+ 4.7 years vs PR− 2.7 ($p = 0.04$). Median time to BM was longer in HER2− 3.2 years vs HER2+ 2.5 years (NS). There was trend towards shorter time to BM in triple negative receptor status in comparison to others ($p = 0.09$). Higher node ratio was a significant risk factor for faster BM ($p = 0.04$). A median time to BM significantly shortened with T stage and was 4.5, 3.4, 2.7 and 1.5 years for T_1-T_4 respectively and also shortened with N stage and was 4.0, 3.0, 1.5 and 1.0 for N_0-N_3, differences were statistically significant ($p < 0.001$). There was no difference in overall survival between patients, whose primary metastatic site was brain or other localization. Increased number of brain metastases had inverse effect on survival, patient's with single BM had a significantly higher 5-year overall survival (75%) in comparison with multiple BM (35%), ($p = 0.03$). Also time from brain metastases to death was longer in single BM ($p < 0.0001$).

Advanced stages of the disease, ER-, PR-, HER2+ are related to higher risk of faster BM. Higher number of BM is related to shorter survival. Major cause of death was brain metastases, therefore further studies are needed for early BM patient's selection.

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RIBBON-1: efficacy of capecitabine-bevacizumab in patients with triple-negative metastatic breast cancer (MBC)

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Background: The RIBBON-1 phase-III study of bevacizumab (A) or placebo was performed in two independently powered cohorts, with patients also receiving capecitabine (X) or taxane/anthracycline. Progression-free survival (PFS; the primary endpoint) was significantly greater with A combined with chemotherapy in both cohorts. The prognosis for patients with ER/PgR/HER2 triple-negative breast cancer is particularly poor. Here we present analysis outcomes from the X cohort of the RIBBON-1 study for patients with triple-negative MBC.

Methods: Recruitment to RIBBON-1 was open to patients with previously untreated, HER2-negative locally recurrent or MBC, with ECOG PS 0 or 1 and no known CNS metastases. In the X cohort, women were randomised (2:1) to X 1,000 mg/m^2 b.i.d. with placebo, or X with A 15 mg/kg q3w, with stratification by disease-free interval ($\leqslant$12 or >12 months), prior adjuvant chemotherapy (yes or no), and number of metastatic sites (<3 or $\geqslant$3). PFS outcomes were analysed in patients with or without triple-negative disease.

Results: The X cohort of RIBBON-1 enrolled 615 patients (XA 409; X-placebo control: 206). Approximately 24% of patients had ER/PgR/HER2 triple-negative disease (XA 21.7%; control 25.3%). In the X cohort overall, a significantly greater improvement in investigator-assessed PFS was achieved with the XA combination (stratified analysis hazard ratio [HR] 0.69 [0.56–0.84], $p = 0.0002$; median PFS 8.6 [XA] vs 5.7 [control] months). In the subgroup of patients with triple-negative disease, PFS appears to be similarly extended with XA (HR 0.72 [0.49–1.06]; 6.1 vs 4.2 months).

Conclusions: MBC patients with triple-negative disease have a poor prognosis and represent a difficult-to-treat population with relatively few therapeutic options. This analysis suggests that the XA combination increases PFS, and so may represent an effective option in this patient group.

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Possible predictive role of prior endocrine therapy on fulvestrant treatment outcome

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Background: Fulvestrant (F) is an estrogen receptor antagonist with no agonist effects that is licensed for the treatment of postmenopausal women with hormone-sensitive metastatic breast cancer (MBC). F use in pretreated MBC patients (pts) is associated with variable response rates. We investigated possible predictive role of treatment delivered prior to fulvestrant.

Material and Methods: From March 2005 to March 2009 124 MBC pts were treated with F at Institute of Oncology Ljubljana, 120 pts were evaluable. The median age of pts was 63 years (range 42−92), median ECOG performance status was 1 (range 0−3). All pts were pre-treated with other endocrine therapy (ET) (including adjuvant), median number of prior ET was 3 (range 1−4): 6/120 (5%) received 1, 52/120 (43.3%) 2 lines, 52/120 (43.3) 3 lines and 10/120 (8.3%) 4 lines of prior ET. The median number of chemotherapy (CT) regimens (including adjuvant)