methotrexate and cytosine arabinoside for CNS metastases and LC and progressed. Before the starting of IT trastuzumab administration, the patient presented with headache, gait disturbance, disequilibrium, dysarthria, neck stiffness and reduced flexion of lower limbs. After the first three doses she recovered lower limb motion, resumed her daily physical activities and CSF cytology has been negative ever since. In January 2009 she started capecitabine and iv trastuzumab for worsening lung metastases, later changed in July 2009 to cisplatin/etoposide/trastuzumab for progressive brain metastases, which she is still on. She refused the placement of an Ommaya reservoir, and weekly LP are still being performed with excellent tolerance. So far the patient has received 50 administrations of IT trastuzumab without adverse events. There was an increase in gadolinium leptomeningeal enhancement over time, which was not associated with functional CNS deterioration; this has faded since cisplatin/etoposide was begun. The patient maintains excellent performance, exercises regularly, performs manual tasks and speaks fluently without dysarthria.

Conclusion: Administration of IT trastuzumab is feasible, safe and led to a dramatic functional improvement in a heavily pre-treated HER2+ MBC patient with LC. Further studies are warranted to confirm clinical activity and optimize trastuzumab delivery into the CNS, including dose, schedule and duration of treatment.

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Efficacy of first-line capecitabine plus bevacizumab in patients with ER/PgR-positive metastatic breast cancer (MBC) and those previously treated with hormone therapy

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Background: The RIBBON-1 phase-III study of bevacizumab (A) or placebo (p) was performed in two independently powered cohorts, with patients receiving capecitabine (X) or taxane/anthracycline. Progression-free survival (PFS), the primary endpoint, was significantly greater with A combined with chemotherapy in both cohorts. In this analysis, we assess the efficacy of first-line X-containing regimens only in women pretreated with hormone therapy.

Methods: Key inclusion criteria were: age $\geqslant$18 years; HER2-negative locally recurrent/MBC; ECOG score 0 or 1. Patients who had received prior chemotherapy for locally recurrent/MBC or with CNS metastases were excluded. Patients were randomised to X 1,000 mg/m^2 b.i.d. on Days 1−14 per 3-week cycle or p, plus A 15 mg/kg q3w, and stratified according to disease-free interval ($\leqslant$12 or >12 months), prior adjuvant chemotherapy (yes or no), and number of metastatic sites (<3 or $\geqslant$3). The primary endpoint of the study was investigator-assessed PFS. The cohort was independently powered to detect a statistically significant increase in PFS at the 0.05 level.

Results: In total, 615 patients were enrolled in the X cohort (XA: 409; Xp control: 206) and 74% of them had ER/PgR-positive status. Around 50% of patients had received prior hormone therapy for early breast cancer (XA 49.6%; control 52.9%) or locally recurrent/MBC (XA 46.0%; control 43.2%). Overall, PFS was significantly greater with the XA combination than Xp (hazard ratio [HR] 0.69, p = 0.0002; 8.6 vs 5.7 months). Subgroup analysis showed that in patients with ER/PgR-positive status, PFS was greater with XA than with control (HR 0.69 [0.55–0.87]; 9.2 vs 6.2 months for XA vs Xp, respectively). Similarly, PFS was greater with XA in the subgroup of patients receiving prior adjuvant hormone therapy (HR 0.71 [0.54–0.93]; 9.5 vs 6.1 months). Analysis of patients with ER/PgR-negative status also revealed an improvement in PFS with XA (HR 0.70 [0.48–1.01]; 6.1 vs 4.2 months), in-line with the significant overall benefit observed in the X cohort.

Conclusions: In the RIBBON-1 study overall, XA combination therapy achieved a significant improvement over Xp in PFS as first-line therapy for HER2-negative MBC. Here, we show that the XA combination provides clinical benefit in patients with hormone-positive or hormone-negative MBC, as well as in those previously treated with adjuvant hormone therapy.

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Characteristics of metastasis in the breast from extramammary malignancies

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Background: Breast metastasis from extramammary neoplasm is rare. We present the cases of metastasis to the breast after review of results in one institute and we want to show the difference of previous report.

Material and Methods: The surgical and pathology databases of Samsung Medical Center from November 1994 to March 2009 were investigated to identify all patients with a diagnosis of metastasis to the breast.

Results: Thirty three patients with breast metastases from extramammary neoplasm were studied. Gastric carcinoma was most common metastatic origin in this study. There were 4 cases with microcalcifications in their metastatic lesions. This is the first report of microcalcification of metastatic lesions to the breast from hepatocellular carcinoma and gastric cancer.

Conclusions: Pathologic examination and considering known clinical history may be helpful to differentiate the primary breast cancer and metastatic cancer. Metastasis to the breast from an extramammary neoplasm usually indicates disseminated metastatic disease and a poor prognosis. An accurate diagnosis of breast metastases, differentiating primary from metastatic breast carcinoma, is important for proper management.

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Bevacizumab (BV) in combination with chemotherapy in the treatment of HER2-negative metastatic breast cancer (mBC): PFS subgroup results from two phase III studies

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Background: Three multicentre, randomised phase III trials of taxane (T), capecitabine (Cap), or anthracycline (Anth) +/− BV established that combination with BV improves progression-free survival (PFS). Outcomes in clinically important subsets are important to demonstrate the consistency of treatment effect and may guide physicians when considering treatment options for patients. Here we compare the activity of BV in various clinically relevant patient subgroups across two phase III studies in mBC.

Methods: Kaplan-Meier methodology was used to estimate median PFS (mPFS) for patient subgroups from the AVADO and RIBBON-1 studies. Patients received BV in combination with docetaxel (D) or placebo (PL) in AVADO and C, T or Anth in RIBBON-1. PFS data based on investigator assessments were used for both trials. For the overall study results, stratified hazard ratios (HRs) are presented with the same stratification factors as the variables that were used for the randomisation, whereas unstratified HRs are presented for the subgroups. Updated data from the April 2009 cut-off (median follow-up 25 months) are shown for AVADO.

Results: In both studies, and in all subgroups shown, an improvement in PFS resulted from combination of BV with chemotherapy.

	AVADO		RIBBON-1			
PFS	PL+D (N = 241)	BV* +D (N = 247)	PL+Cap (N = 206)	BV*+Cap (N = 409)	PL+T/Anth (N = 207)	BV*+T/Anth (N = 415)
Triple-negative disease, n	111		137		142	
Median	6.1	8.1	4.2	6.1	6.2	6.5
HR	0.68		0.72		0.78	
95% CI	0.46–0.99		0.49–1.06		0.53–1.15	
Age $\geqslant$65 years, n	86		153		124	
Median	7.7	10.3	6.2	9.1	8.5	10.1
HR	0.68		0.69		0.83	
95% CI	0.43–1.08		0.47–1.02		0.52–1.34	
Prior adjuvant T, n	77		245		94	
Median	6.7	9.6	4.2	8.7	6.7	9.1
HR	0.51		0.62		0.65	
95% CI	0.32–0.82		0.45–0.84		0.39–1.07	

*15 mg/kg q3w; CI=confidence interval.

Conclusions: Although combination of BV with chemotherapy consistently improved mPFS across a number of clinically relevant subsets, regardless of the chemotherapy backbone used, absolute improvements in HRs and mPFS varied within subsets and across the trials.

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Long term survival and incidence of brain metastasis in HER2-positive (HER2+) metastatic breast cancer patients (MBC) treated with trastuzumab (T): an institutional based review

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Background: HER2+ status is associated with poor prognosis, high incidence of visceral and brain metastasis. However the addition of