or reasons other than progression, endocrine maintenance therapy was allowed until progression. Patients in the ET group were, upon progression, offered 2nd line treatment with capecitabine monotherapy, 2500 mg/m^2 × 14, q3w.

Results: Median TTP was 12.6 (TEX) *vs.* 10.0 (ET) months (HR 0.84; χ^2 2.70, p = 0.10), time on treatment was 6.1 (TEX) *vs.* 5.2 (ET) months (HR 0.73; χ^2 6.87, p = 0.009). Median overall survival was 29.8 (TEX) *vs.* 27.1 (ET) months (HR 0.87; χ^2 0.92, p = 0.34). Response rates for TEX were CR 4.2%, PR 50%, SD 31.3%, PD 8.3%, for ET CR 3.5%, PR 41.3%, SD 35%, PD 14%. Dose intensity (mg/m^2/week) in relation to the starting dosage for TEX were: epirubicin 93.6%; paclitaxel 90.7%; capecitabine 72%, and for ET: epirubicin 95.6%; paclitaxel 94.3%. Seventy of the patients randomized to ET (49%) received capecitabine as 2nd line therapy upon progression. Incidence of grade 3/4 neutropenic fever was similar in both treatment arms, TEX 17.4%, ET 18.9%. Other frequent grade 3/4 side effects due to the TEX regimen were infection (9.7%) and diarrhea (9.7%), and due to the ET regimen neuropathy (10.5%) and infection (9.1%). Symptomatic CHF was reported in 13 cases (4.5%), all of these with accumulated doses of epirubicin exceeding 800 mg/m^2.

Conclusion: TTP was prolonged by 2.6 months in favour of the TEX regimen, although the improvement was not significant. The results of this study reflect the effect of capecitabine on metastatic breast cancer in a comparison of two equitoxic regimens. Since TTP for both treatment arms was longer than anticipated, it is likely that potential differences in outcome may be more obvious in an extended trial.

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Incidence of selected adverse events (AEs) in phase III studies of bevacizumab (BV) in combination with chemotherapy for the treatment of HER2-negative metastatic breast cancer (mBC)

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Background: Three multicentre, randomised phase III trials have demonstrated significant improvements in progression-free survival (PFS) with BV in combination with chemotherapy for the first-line treatment of mBC. E2100 (n = 722) was an open-label trial evaluating weekly paclitaxel (P) +/− BV 15 mg/kg, AVADO (n = 736) was a placebo (PL)-controlled, double-blind trial evaluating docetaxel (D) +/− BV 7.5 mg/kg or BV 15 mg/kg, q3w and RIBBON-1 (n = 1,237) was a PL-controlled, double-blind trial assessing capecitabine (C), taxane (T) or anthracycline (A) +/− BV 15 mg/kg. BV either as a single agent or in combination with chemotherapy has a characteristic safety profile across a number of different tumour types. Selected AEs from two of these phase III mBC trials are summarised to show how different types of chemotherapy affect AE rates in the first-line setting.

Materials and Methods: The NCI-CTCAE v3 was used to record BV-related AEs (grade 3−5 non-haematological events and grade 4/5 haematological events) in AVADO and RIBBON-1. BV-related AEs included arterial thromboembolism (ATE), gastrointestinal perforation, hypertension (HTN), left ventricular systolic dysfunction, venous thromboembolism, proteinuria, bleeding, and wound-healing complications.

Results: Analysing the incidence of known BV-related AEs in the PL arms and BV-containing arms of AVADO and RIBBON-1 we found that HTN ranged from 0−2% for patients (pts) in the PL arms and from 0.8−10% for pts in the BV-containing arms (AVADO: BV 7.5 mg/kg, 0.8%; BV 15 mg/kg, 4.5%; RIBBON-1: C cohort, 9.4%; T cohort, 8.9%; A cohort, 10.0%). For all other BV-related AEs, differences between the PL arms and the BV-containing arms were of smaller magnitude. Treatment discontinuation rates in the BV-containing arms varied across trials, ranging from 11.9–28.3% compared with 4.0–27.0% for the PL arms. In RIBBON-1, treatment discontinuation rates for pts receiving BV were higher relative to the PL arm for the T cohort (7.8% vs. 24.1%) and the A cohort (4.0% vs. 14.3%). There was no difference in treatment discontinuations for pts in the C cohort (11.9% for both arms).

Conclusions: BV in combination with chemotherapy is associated with an increased frequency of selected AEs. Treatment discontinuation rates for AEs vary across trials and may be a function of the chemotherapy agent, dose, and schedule. With the exception of HTN, BV-related grade 3−5 AEs occurred in <5% of pts.

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Final results of a phase II study of combination with nab-paclitaxel, bevacizumab, and gemcitabine as first-line therapy in patients with HER2-negative metastatic breast cancer

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Rationale: Overall response rates (ORR) for patients with HER2-negative (HER2$^-$) metastatic breast cancer (MBC) treated with single-agent solvent based paclitaxel (P) are ~20%. ORR is improved for P + gemcitabine vs. P alone (41 vs. 22%) or P + bevacizumab vs. P alone (37% vs. 21%). Nanoparticle albumin-bound (*nab*)-P resulted in better ORR (42% vs. 27%) than P alone in a phase 3 clinical trial. Therefore, we examined *nab*-P combined with bevacizumab and gemcitabine for first-line treatment of patients with HER2$^-$ MBC.

Patients and Methods: The primary endpoint was PFS; secondary endpoints were ORR, complete (CR) and partial (PR) response rates, clinical benefit (ORR + stable disease), overall survival (OS), and safety. Patients (⩾18 years; HER2$^-$ MBC) received gemcitabine 1500 mg/m^2, nab-paclitaxel 150 mg/m^2, and bevacizumab 10 mg/kg (each administered intravenously over 30 minutes) on days 1 and 15 of a 28-day cycle. Thirty patients were enrolled. One patient was deemed ineligible and was not included in the analysis. Twenty-nine patients (96.6% female, 34 to 69 years, median 54) were treated. Seventeen (58.6%) patients were Hispanic, 8 (27.6%) were African American, 3 (10.3%) were Caucasian, and 1 (3.4%) was Asian. All patients received ⩾1 cycle (median = 6.5, range 2.5 to 23). Estrogen receptor (ER) was present in 55.2% of all cases and progesterone receptor (PR) in 24.1% of patients; 13 (44.8%) patients had triple negative breast cancer (HER2, ER, and PR negative).

Results: Median PFS was 10.4 months (95% CI: 5.6 to 15.2 mo). The ORR was 75.9%, comprising 8 (27.6%) CRs and 14 (48.3%) PRs; 5 patients had minor responses or stable disease, and 2 patients (6.9%) had progressive disease as their best response. The clinical benefit rate was 92.1% (27/29). Of those 13 patients with triple negative disease, 5 (38.4%) had CR; 4 (30.7%) patients had PR; 2 patients had minor response, and 2 patients had progressive disease as their best response. The clinical benefit rate for triple negative patients was 11 (84.6%) of 13. At 24 months, OS was 61.7% (95% CI: 25.4–84.4). Eight (27.6%) patients had grade 3 or 4 toxicity, comprising 1 episode of grade 4 neutropenic fever and the following grade 3 toxicities: 6 episodes of infection; 1 each of leukopenia, thrombocytopenia, peripheral neuropathy, seizure, shortness of breath, hematuria, and tamponade.

Conclusion: First-line combination therapy with *nab*-P, bevacizumab, and gemcitabine demonstrated a 75.9% ORR and median PFS of 10.4 months in this phase II study of HER2$^-$ MBC.

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Capecitabine in older patients ⩾70 yrs with locally advanced or metastatic breast cancer

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Background: Capecitabine (cap) is effective as single agent therapy in metastatic breast cancer (MBC). Its low toxicity and ease of administration make it a potentially good option for elderly patients (pts) but dose reductions are often required. We have therefore retrospectively analysed efficacy and tolerability of cap in elderly pts with locally advanced (LA) or MBC, treated in our Unit.

Materials and Methods: All pts on our prospectively maintained database aged ⩾70 yrs with LA or MBC who were given cap as 1st, 2nd or 3rd line chemotherapy were assessed for response and toxicity according to RECIST criteria and NCI common toxicity criteria, respectively.

Results: Between 12/2001 and 05/2008, 89 pts ⩾70 yrs were given oral cap, 55 (62%) as 1st line and 34 (38%) as 2nd or 3rd line treatment. Thirty-two (36%) pts had soft tissue and/or bone metastases only and 57 (64%) had visceral disease. Planned starting dose of cap was 1000 mg/m^2 twice daily, days 1−14 every 3 weeks. Thirty-six (41%) pts started on 25% dose reduction because of frailty and 12 (13%) pts reduced dose after the 1st or the 2nd cycle. Median number of administered cycles was 6 (range 2−27) and median duration of treatment was 4 (95% CI: 1−19) months. One (1%) complete response (CR) and 39 (44%) partial responses (PR) were seen, for a 45% overall response rate (ORR) (95% CI: 35−55%). A further 19 (21%) pts achieved stable disease (SD) for ⩾6 months. Therefore, disease control (CR+PR+SD) was achieved in 66% of pts. Median time to progression (TTP) and overall survival (OS) were 30

(95% CI: 23−37) and 61 (95% CI: 44−77) weeks (wks), respectively. The ORR for 1st line treatment was 51% compared with 35% for 2nd and 3rd line treatment (p = 0.03). There was no significant difference between 1st and 2nd/3rd line treatment for duration of response (41 vs 55 wks; p = 0.8), TTP (31 vs 21; p = 0.4) or OS (74 vs 52 wks; p = 0.1). No significant difference was seen between pts receiving the full planned dose versus reduced dose for ORR (48% vs 42%; p = 0.9), OS (72 vs 62 wks; p ⩾ 0.9), TTP (27 vs 30 wks; p = 0.5) or duration of response (43 vs 44 wks; p = 0.3). The median OS was 93 (95% CI: 66–120) wks for soft tissue and/or bone metastases vs 49 (95% CI: 39−58) wks for visceral disease (p = 0.03). No significant difference in ORR, TTP or duration of response was seen between these 2 groups. Cap was generally well tolerated, although 35% had treatment delays and 57% required dose reductions. Grade 3−4 hand-foot syndrome toxicity occurred in 11%, lethargy 9% and diarrhoea 2%. No grade 3−4 haematological toxicity was seen except in 5 pts with bone marrow infiltration.

Conclusion: Capecitabine is an effective and well tolerated drug in elderly pts with LA or MBC including for 1st line treatment. Dose reduction is frequently required but does not appear to affect outcome.

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A phase II trial of oral combination chemotherapy with capecitabine and cyclophosphamide (XC) in metastatic breast cancer

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Background: A phase II multicenter trial in patients with metastatic breast cancer (MBC) was conducted to evaluate oral combination chemotherapy (XC) comprising capecitabine (X) and cyclophosphamide (C). We report the results from this trial.

Material and Methods: Patients received XC therapy as follows: 1657 mg/m^2/day (X) plus 65 mg/m^2/day (C), days 1−14, q3w. Patients must have received none or one prior chemotherapy regimen for MBC. The primary endpoint was response rate, secondary endpoints were progression-free survival (PFS) and incidence of adverse events (AEs).

Results: A total of 51 patients (median age 61 years; range 32−82) were enrolled between May 2007 and April 2009. An interim efficacy analysis in 35 patients, showed tumor response to therapy in 16 patients (complete response [CR] in four patients, partial response [PR] in 12 patients), an additional 12 patients achieved stable disease. Progression of disease (PD) was seen in six patients and one patient was non-evaluable (NE). The response rate (RR) was 45.7% with a 54.2% clinical benefit rate (CR + PR + SD ⩾24 weeks). The median PFS was 373 days (range 178–474). A subset analysis suggests that XC therapy is effective even for triple-negative or luminal A (ER+ & HER2−) type breast cancers. An interim safety analysis was conducted in 49 patients. The number of patients who experienced AEs ⩾ grade 3 was: leukocytopenia, 11 patients (22.4%); neutropenia, five patients (10.2%); hemoglobin reduction, one patient (2.0%) and ALP reduction, one patient (2.0%). Grade 2 Hand-foot syndrome (HFS) was reported in 7 patients (14.3%), no grade 3 HFS was reported.

Conclusions: Interim results from this trial demonstrated efficacy of XC oral combination chemotherapy in MBC. In addition, high efficacy of XC was suggested in luminal A type breast cancers and also in triple-negative breast cancers. Adverse drug reactions with XC were mild and the regimen is convenient for patients. Final efficacy and safety results of the trial will be reported at EBCC based on the full follow-up data.

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Quality of life in women with metastatic breast cancer during nine months after randomization in the TEX trial (epirubicin and paclitaxel w/o capecitabine)

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Background: Women with metastatic breast cancer have a relatively short expected survival. Therefore, the impact of treatment on quality of life is an important factor to consider. In the TEX trial, two first line treatment regimens were compared in patients with metastatic breast cancer.

The aim of this paper is to compare the effects of two treatment regimens in the TEX trial on HRQOL at two assessment points (2 and 9 months after random assignment).

Material and Methods: A total of 287 patients at ten Swedish hospitals were randomized to treatment with either epirubicin plus paclitaxel (ET, 143 patients) or epirubicin, paclitaxel and capecitabine (TEX, 144 patients). Treatment was given in 3-week cycles.

Health related quality of life (HRQOL) was assessed by the EORTC-QLQ C30 and EORTC QLQ-BR23 questionnaire at 3 points during nine months from randomization.

Results: 163 patients (70%) completed the questionnaire at baseline, and 2 and 9 months after random assignment. There were no statistical significant differences between the TEX group and the ET group on any of the subscales two months after randomization. Small clinical differences (5 to 10 points difference) were found for Global quality of life, Role functioning, Social functioning and Insomnia, favouring patients treated with ET. This group also scored lower on Fatigue, Dyspnoea, and Diarrhoea than patients who received TEX, although the differences were small. At the nine months assessment, the TEX group scored statistically significantly higher on Global quality of life and Physical functioning. No other statistically significant differences were found for any of the subscales analyzed. In contrast to the findings at the two months assessment, small clinically significant differences were found for Global health related quality of life, Physical functioning, Role functioning, Emotional functioning, Dyspnoea, and Insomnia, all in favor of the TEX group.

Conclusions: At the time when side-effects of chemotherapy were present, patients treated with the combination TEX appeared to fare a bit worse than those receiving ET. However, after nine months, when the patients had adapted to treatment, the TEX group seemed to have a slightly better quality of life.

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First results of an international, retrospective observational study of metastatic breast cancer patients treated with oral vinorelbine based-chemotherapy

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Background: Full oral Chemotherapy (CT) is an active and convenient therapeutic option for metastatic breast cancer (MBC) patients (pts). In this retrospective analysis, we reviewed the characteristics and the outcome of pts treated by oral vinorelbine either as a single-agent or in combination with capecitabine as a first or second line chemotherapy in the metastatic setting.

Materials and Methods: We analysed 216 MBC pts who started treatment with a full oral CT in 13 centres and 7 countries between 2006 and 2008. To be eligible, pts must have received either as a 1st (56%) or 2nd (44%) line oral vinorelbine as a single agent (54%) or in combination with capecitabine (46%).

Results: Main pts characteristics in the full population (n = 216): median age (range): 61 years (32−87); categories of age: <50: 18%, 50−65: 44%, ⩾65: 38%; hormone receptor positive: 63%; ⩾2 metastatic sites: 58%; visceral metastases: 49%; prior CT: 86%; prior CT for MBC: 44%; prior anthracycline: 69%; prior taxane: 43%; prior anthracycline + taxane: 38%; prior hormone therapy: 63%. Median number of cycles: 6 (range:1−54); 52% of pts received more than 6 cycles. G3/4 toxicities: neutropenia 8%, anaemia 2%, thrombocytopenia 1%, febrile neutropenia/neutropenic infection 2%, nausea 6%, vomiting 4%, diarrhoea 6%, fatigue 6%, hand-foot syndrome 14% (combination with capecitabine), neuropathy 1%, alopecia (grade 2) 1%. Efficacy: disease control rate 77% (95% CI [71−83]), 74% as single-agent, 81% in combination, 82% in 1st line, 71% in 2nd line. Median progression-free survival was 9.7 months (95% CI [8.2–12.6]) in 1st line and 6.6 months (95% CI [5.5−8.5]) in 2nd line. With a median follow up of 17.5 months (1st line) and 14.5 months (2nd line), 128 patients were alive, 34 pts were lost to follow-up and 54 pts were dead at the time of