were delivered. In arm A, 16.7% of the patients had one or more cycles delayed due to side effects, compared with 19% in arm B and 2.5% in arm C. 23.8% of the patients in arm A experienced a grade 3 infection or febrile neutropenia compared to 4.7% and 15% in the B and C arm respectively, a retrospective calculation of events in relation to possible events (cycles) resulted in 3.6% (arm A), 0.6% (arm B) and 3.1% (arm C) events per cycle.

An amendment (an extra week between the EC and T parts) was introduced after 124 cycles in the A and B arm due to six grade 3 hand-foot-skin reactions during the docetaxel part. After the amendment, one grade 3 event occurred in the EC and T arm, respectively, in 496 cycles. In the A and B arm, 28.6% (12 in each arm) of the patients were hospitalized due to side effects and the corresponding figure in the C arm was 20% (8 patients).

Conclusion: The concept of dose-dense and tailored EC/T is manageable and is presently studied in a randomized phase III study together with the Austrian Breast and Colorectal Study Group (SBG 2004−1/ABCSG-25).

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Safety data from a phase II study of neoadjuvant bevacizumab and trastuzumab administered with albumin bound paclitaxel (nab paclitaxel) and carboplatin in HER2+ locally advanced breast cancer

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Background: SPARC is a known prognostic factor for poor survival and its expression has been shown to increase with tumor aggressiveness. Preclinical evidence suggest that SPARC may mediate enhanced intratumoral accumulation of albumin-bound paclitaxel (Abraxane®, *nab*-paclitaxel) through its interaction with albumin. In a prior phase III study of patients with metastatic breast cancer, *nab*-paclitaxel resulted in higher response rate and an increased time to progression compared with standard solvent-based paclitaxel. The addition of biologic targeted therapies added to standard chemotherapy in breast cancer has translated into improved outcomes. This multicenter phase II pilot study was designed to evaluate the feasibility, toxicity, and preliminary efficacy of dual VEGF and HER2 monoclonal antibody receptor blockade with bevacizumab (B) and trastuzumab (T) administered in combination with neoadjuvant *nab*-paclitaxel and carboplatin.

Methods: Eligibility: cT1−4, N0−3, M0 adenocarcinoma (T1N0M0 excluded), FISH HER2+, normal LVEF, ECOG PS $\leqslant$ 2, adequate organ function, controlled hypertension (HTN), neuropathy $\leqslant$ grade 1, tumor tissue availability for SPARC testing. Treatment: Nab-paclitaxel 100 mg/m^2 days 1, 8, 15 q28 days with carboplatin AUC of 6 day 1 q28 days $\times$ 6 cycles, B 5 mg/kg qwk $\times$ 23 wks with T 4 mg/kg loading dose followed by 2 mg/kg qwk $\times$ 22 wks. Surgery $\geqslant$4 wks following last B. T at 6 mg/kg and B 15 mg/kg q3wk post op for a total of 1 year (B reinitiated $\geqslant$4 weeks post op). LVEF measurements at baseline, 3, 6, 12, and 18 months. SPARC immunohistochemistry assessments were performed and scored on a 0−3 level (0 = absent, 1 = weak, 2 = moderate, 3 = strong).

Results: 25 pts are evaluable for toxicity. Histology: ductal 80%, lobular 12%. 48% ER and PR negative, ECOG PS 0 – 90%. Grade 3/4 hematological toxicity in >5% of patients consisted only of neutropenia in 12 pts (48%). Nonhematologic toxicity was only notable for grade 3 hypertension in 3 pts (13%). No LVEF dysfunction was noted. 4 pts went off study: 2 − pt wishes, 2 – toxicity (fatigue, reflux). 2 pts did not complete post operative maintenance therapy (unrelated to treatment).

Conclusion: Neoadjuvant dual monoclonal antibody receptor blockade with bevacizumab plus trastuzumab in combination with *nab*-paclitaxel and carboplatin is feasible. No unexpected toxicities and no early evidence of LVEF dysfunction have been reported. SPARC tumor assessments are ongoing and will be presented.

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Concurrent or sequential adjuvant hormonoradiotherapy after conservative surgery for early-stage breast cancer: first results of the CO-HO-RT phase II randomized trial

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Background: We recently showed in an aromatase-gene transfected breast cancer cell line, a radiosensitizing effect of letrozole. We then conducted a multicentric phase II randomized trial evaluating adjuvant concomitant radiotherapy and letrozole with radiotherapy followed by letrozole in postmenopausal early breast-cancer patients (CO-HO-RT trial).

Methods: Postmenopausal pts with early-stage breast cancer were randomized after conservative surgery to either: A) concurrent RT-LET (LET started 3 weeks before the first day of RT) or B) sequential RT-LET (LET started 3 weeks after the end of RT). Whole breast RT was delivered to a total dose of 50 Gy +/− a 10−16 Gy boost. Pts were stratified by center, adjuvant chemotherapy (ACT), boost, CD8 radiation-induced apoptosis. Primary endpoint was radiation-induced acute and late skin toxicity. Skin toxicities were evaluated by two different clinicians at each medical visit (CTCAE v3.0). Lung CT-scan and functional pulmonary tests were performed regularly. Quality of life and cosmetic assessments were registered. DNA samples were screened for SNPs in the ATM genes.

Results: A total of 150 pts were randomized between 01/05 and 02/07. Median follow-up was 17 months (range, 6−49). No statistical differences were identified between the two arms in terms of mean age; initial TNM; median surgical bed volume; post surgical breast volume. ACT and RT boost were delivered in 19% and 38% of pts, respectively. Overall, 10 patients (6.7%) presented grade 3 acute skin dermatitis during RT without differences between both arms. Grade 2 acute skin dermatitis were observed in 36.5% and 32% in arm A and B, respectively but symptoms rapidly settled in most patients by months 3, 6, and 12. Grade 2 radiation-induced subcutaneous fibrosis were found in 8 patients (5%) with a slight difference in disfavor of arm B (7%) vs 4% in arm A. Three patients (2%) presented a grade 2 pneumonitis (all in arm A). Overall, quality of life and cosmesis were good to excellent.

Conclusions: Concurrent or sequential adjuvant radiohormonotherapy with letrozole is feasible in daily practice. Identifying hypersensitive patients with CD8 RIA or ATM screening will help tailoring treatments.

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Relationship between estrogen receptor (ER) status and efficacy of postoperative adjuvant chemotherapy with oral tegafur-uracil (UFT) or CMF: subset analysis from a randomized controlled trial (CUBC trial in Japan)

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Background: It has been reported that UFT decreased the risk of relapse by 21% in patients with Stage I to III breast cancer and risk of mortality by 35% in patients with node-negative breast cancer (Kasumi *et al*., Oncology 2003; Noguchi *et al*., J Clin Oncol 2005). We previously reported three-year follow-up data from a randomized comparative study comparing classical CMF (6 courses) plus tamoxifen (TAM) with UFT (2 years) plus TAM in patients with operable node-positive breast cancer (Inaji *et al*., ASCO 2004). We now report a five-year follow-up data and the relationship between estrogen receptor (ER) status and the efficacy in each treatment group.

Materials and Methods: A total of 350 patients, 173 patients in the CMF + TAM group [CPA 65 mg/m^2 (po): days 1 to 14, MTX 40 mg/m^2 (iv):