of contralateral breast cancer was 1.53-fold higher (95% CI 1.05−2.24, p = 0.03) in radiotherapy arms.
Conclusion: Radiation therapy should follow lumpectomy in women with localized, mammographically detected DCIS. Our findings in 3665 patients strongly confirm that radiotherapy substantially reduces invasive and DCIS ipsilateral breast cancer recurrence risk after breast-conserving surgery. No data are currently available to identify a subgroup of women with the kind of DCIS who did not need to be treated with radiation therapy.

2030 ORAL

Efficacy of neoadjuvant trastuzumab in patients with inflammatory breast cancer: data from the NOAH (NeOAdjuvant Herceptin) Phase III trial

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Background: There is currently no standard therapy for women diagnosed with HER2-positive inflammatory breast cancer (IBC), a rare and highly aggressive disease typically treated with neoadjuvant chemotherapy. Here we present data from patients (pts) with HER2-positive IBC included in the randomised Phase III NOAH (NeOAdjuvant Herceptin) trial of neoadjuvant trastuzumab (Herceptin®; H) in combination with chemotherapy.
Methods: Pts with locally advanced breast cancer at first diagnosis were recruited and assigned to 1 of 2 cohorts depending on HER2 status. All pts received neoadjuvant chemotherapy: 3 cycles of doxorubicin–paclitaxel (AT: A 60 mg/m^2, T 150 mg/m^2 q3w), 4 cycles of T (175 mg/m^2 q3w) and 3 cycles of cyclophosphamide/methotrexate/5-fluorouracil (CMF: C 600 mg/m^2, M 40 mg/m^2, F 600 mg/m^2 q4w on days 1 and 8). Pts with HER2-positive disease were randomised to receive concomitant H (8 mg/kg iv loading dose then 6 mg/kg q3w for 1 year) or chemotherapy only. The first pre-planned interim efficacy analysis evaluated the primary end point of event-free survival and secondary end points of in-breast pathological eradication (pCR), in-breast and nodal pathological eradication (tpCR), objective clinical response rate (cRR) and safety.
Results: 61/228 pts with HER2-positive disease and 14/99 with HER2-negative tumours had IBC; 31 of the pts with HER2-positive IBC received chemotherapy with H.

	HER2-negative IBC	HER2-positive IBC	
	(n = 14)	−H (n = 31)	+H (n = 31)
cRR, %	57.1	77.4	77.4
pCR, %	28.6	19.3	54.8*
tpCR, %	28.6	12.9	48.4**

*p = 0.004; **p = 0.002.

The cRR was similar with or without H in pts with HER2-positive IBC, but addition of H significantly improved the pCR and tpCR rates compared with chemotherapy alone (54.8% vs 19.3%, p = 0.004; 48.4% vs 12.9%, p = 0.002). There were no reports of left ventricular ejection fraction decreases to <45% and only 5/47 pts receiving H had absolute decreases of ⩾10%.
Conclusions: Addition of H to neoadjuvant chemotherapy more than doubled the rates of pCR and tpCR in pts with HER2-positive IBC compared with chemotherapy alone. At the low cumulative dose of administered anthracycline (total doxorubicin dose of 180 mg/m^2), the chemotherapy regimen was well tolerated with no reported symptomatic cardiac events by the time of this interim analysis.

2031 ORAL

A comparison between HER2, p53, PAI-1, angiogenesis and proliferation activity as prognostic variables in tumours from 408 patients diagnosed with early breast cancer

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Background: The prognostic potential of HER2, p53, PAI-1 tumour tissue protein level, angiogenesis and proliferation activity (expressed by MIB-1 estimates) were investigated in tumours from 408 patients diagnosed with early breast cancer and followed >10 years. 167 patients (41%) had died from cancer.
Materials and Methods: Using immunohistochemistry tumours were stained for anti-HER2, anti-p53, anti-CD34, and anti-MIB-1, whereas PAI-1 was measured by ELISA. A HER2 score of 3+ was considered positive, and in cases of HER2 score of 2+ a FISH analysis for amplification was performed. p53 was scored in quartiles according to the density of tumour cells staining positive. Angiogenesis was evaluated by the Chalkley technique, using the hot spot approach, whereas MIB-1 estimates were based on systematic random sampling.
Results: Eighty-six tumours (21%) were HER2 positive. The distribution of p53 in classes 1 through 4 was 31, 104, 75 and 198 cases, respectively. Median PAI-1, Chalkley and MIB-1 was 0.72 ng/mg protein (range, 0−90 ng/mg protein), 5.00 (range, 2.67−12.00) and 15% (range, 1−83%), respectively. A high MIB-1 tertile was correlated with HER2 positivity (P < 0.0001), high scores of PAI-1 (P = 0.002), Chalkley count (P < 0.0001) and p53 score (P < 0.0001). None of the factors were otherwise inter-correlated. In univariate analyses with disease-specific survival (DSS) as endpoint, HER2 positivity (P < 0.0001), and increasing values of Chalkley count (P = 0.006), MIB-1 (P = 0.004) and PAI-1 level (P = 0.06) were prognostic markers. Among the 191 node-negative patients, HER2 positivity (P < 0.0001), high PAI-1 levels (P = 0.006) and postmenopausal status (P = 0.03) were associated with poor DSS. In the 217 node-positive patients, HER2 positivity (P = 0.0003), high value of MIB-1 (P = 0.02), Chalkley (P = 0.003), negative estrogen receptor (P = 0.0004) and high malignancy grade (P < 0.0001) were indicators of poor DSS. In multivariate analysis increasing number of metastatic lymph nodes (RR 2.02, 95% CI 1.67−2.44), HER2 positivity (RR 1.96, 95% CI 1.38−2.77), increasing PAI-1 (RR 1.05, 95% CI 1.02−1.07) and high malignancy grade (RR 1.28, 95% CI 1.02−1.61) showed independent prognostic value. In node-negative patients the HER2 status was an even stronger independent prognosticator with a RR 3.42, 95% CI 1.81−6.47.
Conclusion: Compared to p53, PAI-1, Chalkley counts and MIB-1, HER2 positivity was the strongest independent marker of poor prognosis, irrespective of lymph node status.

2032 ORAL

Detection of minimal residual disease (MRD) in peripheral blood of primary breast cancer patients – Translational research in the SUCCESS-Study

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Background: Patients with the detection of MRD in bone marrow are known to have an increased risk for recurrence and a poorer clinical outcome. However, peripheral blood would be the preferable compartment to monitor treatment efficacy due to increased feasibility. The translational research program of the German SUCCESS-trial was established to evaluate MRD in peripheral blood at 4 different time points during adjuvant systemic treatment of breast cancer patients.
Here first results of the detection of MRD at primary diagnosis and after adjuvant chemotherapy will be presented.
Materials and Methods: Cells were separated by Oncoquick® (greiner bio-one, Frickenhausen, Germany) followed by labelling of epithelial cells with

the anti-cytokeratine-antibody A45-B/B3 (Micromet, Munich, Germany), directed against cytokeratines 8, 18 and 19, and immunohistochemically staining with neu-fuchsin. All preparations were screened by two independent persons.
Results: 328 breast cancer patients were analyzed at primary diagnosis. Among those, 133 patients returned for a second blood sampling after completion of adjuvant chemotherapy. Most of the tumors were small (43% pT1, 51% pT2, 4% pT3, 1% pT4) but of intermdediate or unfavourable grade, (G1 4%, G2 46%, G3 42%). 66% of the patients were node-positive (34% pN0, 38% pN1, 20% pN2, 8% pN3) and a positive hormone receptor status was seen in 71%. In 22% the Her2-status was positive. MRD in peripheral blood was found in 31% of all patients before and in 9% after chemotherapy. The mean number of detected cells was 2 (range 1−9). 87.2% of patients who showed MRD at the first measurement turned negative after chemotherapy.
Neither tumor size ($p = 0.624$), lymph node metastases ($p = 0.450$), histopathological grading ($p = 0.168$), hormone receptor status ($p = 0.270$) or Her2/neu-status of the primary tumor ($p = 0.893$) correlated with the presence of MRD.
Conclusions: The detection of MRD in peripheral blood can be widely used and is suitable for repeated measurements. Further follow-up will show, if this method can be used for risk stratification and monitoring of treatment efficacy in adjuvant breast cancer.

2033 ORAL

Improved chemotherapy delivery in breast cancer patients receiving pegfilgrastim primary prophylaxis compared with current practice neutropenia management – results from an integrated analysis (NeuCuP)

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Background: Chemotherapy (CT) dose reductions and delays due to neutropenia or febrile neutropenia (FN) may worsen clinical outcomes. FN prophylaxis with granulocyte colony stimulating factor (G-CSF) can help to maintain planned CT dosing schedules. Recent EORTC/ASCO guidelines recommend routine growth factor primary prophylaxis (PP) for patients with overall $\geqslant$20% FN risk. An aim of this integrated analysis of individual patient data was to assess CT delivery in breast cancer patients receiving a range of CT regimens supported by PP pegfilgrastim or any G-CSF according to current practice (CP).
Methods: Studies involving breast cancer CT regimens with moderate (15–20%)/high ($\geqslant$20%) risk of FN were identified by literature review. For this integrated analysis, individual patient data were available from 8 clinical trials and 3 observational studies (conducted 1998–2005) involving these regimens and PP use of pegfilgrastim (6 mg dose in all cycles) or CP neutropenia management (no G-CSF or pegfilgrastim/daily G-CSF in any cycle). Outcome measures reported here are CT dose delays/reductions, hospitalizations, and anti-infective use.
Results: 2282 patients were analyzed (PP: 1303; CP: 979). The mean age ($\pm$SD, years) was 51.4$\pm$10.4 for PP vs 52.0$\pm$9.9 for CP; 28% vs 28% of patients had Stage IV disease, 97% vs 85% had ECOG status 0–1 (11% missing in CP) and 30% vs 37% had prior chemo/radiotherapy. The most common regimens were docetaxel (37% vs 50%), TAC (31% vs 27%), and ADoc (27% vs 3%). In cycle 1, 75% of CP patients did not receive any G-CSF, 12% received pegfilgrastim, and 12% received various daily G-CSF regimens (11% of whom had <5 doses, 50% had an unspecified number of doses). Dose delays/reductions for the PP and CP groups are shown in the table, as well as hospitalizations and anti-infective use.

	PP, % patients (95% CI) (n = 1303)		CP, % patients (95% CI) (n = 979)	
	Overall	Cycle 1	Overall	Cycle 1
Dose delay >3 days in any cycle	15 (13, 17)	N/A	16 (14, 19)	N/A
Dose reduction $\geqslant$15% in any cycle	9 (7, 10)	N/A	24 (21, 27)	N/A
FN-related hospitalization	4 (3, 5)	3 (2, 4)	10 (8, 12)	6 (5, 8)
Use of anti-infectives[a]	42 (40, 45)	22 (20, 25)	55 (52, 58)	43 (40, 46)

[a]210 PP and 248 CP pts were prescribed prophylactic antibiotics in original protocol.

Conclusions: In this analysis of patients receiving CT with moderate/high FN risk, PP pegfilgrastim supported a higher level of CT delivery than CP neutropenia management. PP pegfilgrastim also reduced the number of FN-related hospitalizations.

Poster presentations (Wed, 26 Sep, 14:00−17:00)
Breast cancer – early disease

2034 POSTER

Weekly docetaxel vs CMF as adjuvant chemotherapy for elderly breast cancer patients: safety data from the ELDA trial

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Background: we are conducting a phase 3 study to compare weekly docetaxel vs CMF as adjuvant treatment of elderly breast cancer patients (the ELDA trial, cancertrials.gov ID: NCT00331097). An amendment has been approved in December 2006 to modify methotrexate dose according to creatinine clearance. We have compared safety data collected before the amendment.
Patients and Methods: early breast cancer patients, 65 to 79 years old, are eligible if they have metastatic lymphnodes or average to high risk of recurrence according to 2001 St.Gallen criteria, PS 0−2, adequate bone marrow, renal and hepatic function. Patients are randomly assigned to CMF (cyclophosphamide 600 mg/m^2, methotrexate 40 mg/m^2, fluorouracil 600 mg/m^2, days 1−8) or docetaxel (35 mg/m^2 days 1−8-15), both every 4 weeks.
Results: data of 101 patients enrolled up to October 2006 were analysed: 53 in the CMF and 48 in the docetaxel arm. Median age was 70 years. At least one grade 3−4 toxic event of any type was reported in 40 (75.5%) and 19 (39.6%) patients with CMF and docetaxel, respectively (exact $p = 0.0002$). Grade 3−4 hematological events were observed in 37 (69.8%) vs 4 (8.3%) cases (exact $p < 0.0001$) and grade 3−4 non-hematological toxicity in 12 (22.6%) vs 15 (31.2%) patients (exact $p = 0.11$), with CMF and docetaxel, respectively. In particular, a significantly higher incidence of anemia, neutropenia, thrombocytopenia and febrile neutropenia was reported in CMF arm. Among non-hematological toxicity, constipation, mucositis, nausea and vomiting were significantly more common with CMF; diarrhoea, abdominal pain, dysgeusia, neuropathy and liver toxicity were significantly more frequent in docetaxel arm. No significant interaction was found between severe toxicity and baseline variables, including creatinine clearance and geriatric assessment.
Conclusions: in the present analysis, weekly docetaxel was less toxic than CMF. Efficacy data must be awaited to draw conclusions on the role of adjuvant weekly docetaxel for elderly early breast cancer patients.

2035 POSTER

NEAT-A: Accelerated sequential epirubicin followed by higher dose 14 day CMF, using pegfilgrastim, is a feasible alternative for delivering dose dense E-CMF chemotherapy in early breast cancer

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Background: E-CMF [epirubicin (E) $\times$ 4 cycles every (q) 21 days (d), followed by either classical CMF $\times$ 4 cycles q 28d or higher dose CMF q 21d] is established as highly effective adjuvant chemotherapy for early breast cancer (EBC), reducing mortality by 30% compared with CMF alone [Poole NEJM 2006]. Dose dense anthracycline-taxane schedules, accelerated with GCSF support, have been shown to be superior to conventional regimens [Citron JCO 2003, Burnell SABCS 2006]. Exploration of accelerated E-CMF is therefore of considerable interest. We