Table 1. Prognostic factors in stage II breast carcinomas compared with 5-year survival

Prognostic factors	Univariate		Multivariate	
	RR (95% CI)	p	RR (95% CI)	p
p53+	3.71 (1.17–11.77)	0.026	0.67 (0.17–2.67)	0.57
Inadequate anthracyclines dose	4.54 (1.22–16.89)	0.024	5.19 (1.19–22.57)	0.028
ER-	4.68 (1.02–21.45)	0.047	4.38 (0.79–3.373)	0.091

38LBA LATE BREAKING ABSTRACT

Therapy monitoring of sorafenib effect on experimental prostate carcinomas by dynamic contrast-enhanced MRI

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Background: To investigate and quantify the effects of the multikinase inhibitor sorafenib on experimental prostate carcinomas in rats by dynamic contrast-enhanced MRI assays of endothelial permeability and tumor vascularity.
Methods and Materials: 16 Copenhagen rats implanted with subcutaneous prostate carcinoma allografts (MLLB-2) were imaged at baseline and after a one-week treatment course of sorafenib via gavage by dynamic MRI at 3.0T following enhancement with a prototype macromolecular contrast agent [albumin-(Gd-DTPA)]. Quantitative MRI estimates of tumor microvessel permeability (transfer constant K^{PS}, 10^{-3} min^{-1}) and tumor vascular richness (blood volume; %) were calculated with PMI 0.4 software based on a two-compartment kinetic model.
Results: Sorafenib significantly suppressed endothelial permeability and blood volume in prostate carcinoma allografts over the treatment course of one week. In sorafenib-treated tumors (n = 8) the transfer constant K^{PS} yielded a significant decrease in endothelial permeability from baseline to day 7 (baseline K^{PS} = 0.62±0.20, day 7 K^{PS} = 0.08±0.09; p < 0.01). The blood volume in sorafenib-treated tumors decreased significantly over the treatment course (baseline BV = 5.1±1.0, day 7 BV = 0.56±0.48; p < 0.01). In the control tumors without treatment (n = 8), neither the transfer constant nor the blood volume changed significantly.
Conclusion: Sorafenib, a known inhibitor of angiogenesis in renal and liver cancer, significantly reduced endothelial permeability and tumor vascularity in a prostate cancer model as assayed by dynamic MRI enhanced with macromolecular contrast media. Dynamic MRI enhanced with macromolecular contrast media could prove valuable for monitoring the anti-angiogenic effect of sorafenib on an individual patient basis.

39LBA LATE BREAKING ABSTRACT

Preoperative serum CA 15−3 and CEA in women with breast cancer and their relationship with relapse of the disease

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Background: The aim of this retrospective study was to investigate whether the preoperative CA 15−3 and CEA serum levels are able to predict patients who may have a shorter disease free survival interval after curative surgery in women with breast cancer (BC).
Materials and Methods: We retrospectively reviewed a series of 363 consecutive postmenopausal women (median age 63 years, range 47−89 years) with pT1−2, N0−1 BC who were followed-up for at least 36 months after lumpectomy or mastectomy. Two Groups of patients were considered: Group 1 (age 47−64 years), 203 (55.9%) patients; Group 2 (age >64 years), 160 (44.1%) patients. The greater diameter of the tumor (pT) did not differ between Groups (19.9±13.6 vs. 22.7±14.0 mm, p = 0.06), while the preoperative CA 15−3 and CEA serum levels were higher in older patients: 19.0±14.3 vs. 24.9±27.3 U/L (p = 0.01), and 2.7±8.5 vs. 4.8±11.0 ng/mL (p = 0.04), respectively.
Results: During follow-up (36−60 months) 62 (17.1%) patients developed relapse (DR) of the disease (41 and 20 among Groups 1 and 2, respectively), while 301 (82.9%) were disease-free (DF). Group 1: baseline CA 15−3 serum levels: (DF) 25.0±11.4 (DF) vs. (DR) 31.4±14.6 U/L (p = 0.003); baseline CEA serum levels: (DF) 5.9±4.8 vs. (DR) 7.4±6.4 ng/mL (p = 0.099). Group 2: baseline CA 15−3: (DF) 27.3±13.2 vs. (DR) 20.4±6.5 U/L (p = 0.023); baseline serum CEA levels: (DF) 6.6±5.2 vs. (DR) 3.7±2.5 ng/mL (p = 0.015).
Conclusions: Surprisingly, in the subgroup of older patients with relapse (DR), both CA 15−3 and CEA serum levels were lower than in the subgroup of disease-free patients (DF). We conclude that, although serum tumor markers levels should be useful during follow-up, their baseline levels are not useful in predicting relapse in elderly patients with BC.

40LBA LATE BREAKING ABSTRACT

Results of an RCT investigating the cost-effectiveness of four follow-up strategies after breast cancer

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Background: The cost-effectiveness of frequent follow-up (f-up) visits after treatment for breast cancer is debated. Therefore, we conducted a multicenter RCT (ISRCTN 74071417) to determine the costs and effects of four f-up strategies, investigating hospital f-up, nurse-led telephone f-up, and an educational group program (EGP).
Method: Between 2005 and 2008, 320 breast cancer patients were randomized into one of four f-up strategies for their first year after treatment: 1. hospital f-up; 2. nurse-led telephone f-up; 3. hospital f-up with EGP; 4. nurse-led telephone f-up with EGP. The EGP consisted of two group-sessions, led by a breast care nurse and health psychologist, in which physical and psychosocial sequelae of diagnosis and treatment were discussed.
Costs and effects of the four f-up strategies were compared to determine the most cost-effective strategy. Costs were calculated from a societal perspective, thus included healthcare costs (e.g. outpatient clinic visits, laboratory tests, diagnostic imaging), patient costs, and productivity losses. Effects were expressed as quality-adjusted life-years (QALYs), measured by the EQ-5D. Data were collected at baseline, three, six, and 12 months after treatment. Non-parametric bootstrapping with 1000 replications and one-way sensitivity analyses were used to assess the uncertainty in costs and effects.
Results: Nurse-led telephone f-up with EGP (f-up strategy 4) was the cheapest and most effective f-up strategy. Mean annual costs per patient were €3003 and this strategy yielded 0.771 QALYs. Mean annual costs per patient and mean effects for hospital f-up (f-up strategy 1) were €3603 and 0.750 QALYs. Mean costs and effects for nurse-led telephone f-up (f-up strategy 2) were €3933 and 0.766 QALYs, and for hospital f-up with EGP (f-up strategy 3) €3281 and 0.746 QALYs. Hence, in the incremental cost-effectiveness analysis, nurse-led telephone f-up with EGP dominated all other f-up strategies. Uncertainty analysis showed that the probability of this dominance ranged between 62& and 70% for different QALY threshold values. Furthermore, sensitivity analyses with a range of cost prices for hospital visits (€50−200) and telephone f-up (€10−50) showed that cost-effectiveness results were robust.
Conclusion: Nurse-led telephone f-up with an educational group program is the most cost-effective f-up strategy out of four different f-up strategies for the first year after breast cancer.

41LBA LATE BREAKING ABSTRACT

Single institute phase II study of weekly cisplatinum and metronomic dosing of endoxan and methotrexate in second line metastatic breast cancer triple-negative

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Background and Introduction: Triple negative breast cancer is a disease prevalent in developing countries and non caucasian population. There is no standardized treatment options available include using combination chemotherapy with biologics, novel drugs results of which are of limited overall survival at prohibitive costs. This study involves the use of weekly cisplatinum with metronomic dosing of cyclophosphamide and intermittant methotrexate.

Material and Method: 126 patients between age group of 38 to 72 years were enroled in the trial cleared by the Institutional IRB. Patients who had already received anthracyclines and taxanes and had relapsed, could not afford exbepalione and/or avastin. Patients who were analised for ER/PR and HER-2NEU. Only patients negative for all 3 were enrolled. Routine biochemical estimations and imaging were done. VEGF and CRP were estimated every 8 weeks.
Patients were randomised to either endoxan 50 mgt per day at 10 am and methotrexate 2.5 mg twice a day at 9 am and 5 pm with or without cisplatinum. Patients were stratified by number of sites of metastasis and with or without visceral metastasis with or without bisphosphonates.
Chemotherapy was continued till progression of disease or toxicity. Patients were evaluated every 8 weeks for response and every week for toxicity.
Results: The average age of patients was 58 years. 66 patients on no platinum arm and 60 patients on platinum arm. The response rate in the no platinum arm was 30% and in the platinum arm was 62%. The time to progression was 7 months in no platinum arm and 13 months in platinum arm. Median overall survival was 12 months vs 16 months.
Patients who received bisphosphonates showed better response and survival. Patients with visceral disease and more than 2 sites of metastasis did better with platinum. Response and survival was related to baseline C-Reactive Protein and VEGF and drop by 50% at the end of 8 weeks.
Conclusions:
1. Visceral metastasis and more than 2 sites of metastasis are bad prognostic markers
2. Raised CRP more than 3 times of baseline and VEGF more than 8 times of baseline are bad prgnostic markers.
3. Drop in CRP and VEGF at 8 weeks more than 50% was a good marker
4. Cisplatinum weekly with metronomic Endoxan and methotrexate is a excellent combination for triple negative disease from efficacy as well as cost.

42LBA LATE BREAKING ABSTRACT

Anthracycline-rechallenge using pegylated liposomal doxorubicin (PLD) in patients with metastatic breast cancer (MBC): a meta-analysis using pooled individual data from 4 prospective trials

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Background: Few data are available on the efficacy of anthracycline rechallenge using PLD.
Methods: Pooled individual data from 4 trials (Keller, J Clin Oncol 2004; O'Brien, Ann Oncol 2004; Al-Batran, Br J Cancer 2006; Al-Batran, Oncology 2006) were used to examine the activity of PLD in pts with MBC, pre-treated convential anthracycline (CAC). Primary endpoint was clinical benefit rate (CBR), defined as objective response or stable disease, both lasting $\geqslant$6 months. CBR was assessed in the entire group (primary hypothesis CBR $\geqslant$30%) and in pre-defined subgroups of pts; depending on the most important features of their prior anthracycline-based therapy.
Results: The studies comprised a total 935 pts, of whom 274 pts had received PLD after prior exposure to conventional anthracyclines. At the time of PLD therapy, these (274) pts were heavily pre-treated (median lines of previous chemotherapy 4; range 1 to 9; 93.4% of pts received PLD after $\geqslant$2 previous chemotherapies). Prior CAC treatment was adjuvant, anti-metastatic, or both in 14%, 46%, or 40% of pts, respectively. The overall CBR from PLD was 32.2% (95% CI, 26.7–37.8%), with no difference between pts who were considered anthracycline resistant (defined based on the study records) and those who were not (31.9 v 31.6%, respectively, p = 1). There also was no difference in CBR from PLD between pts who received prior CAC adjuvant only (33.3%), anti-metastatic only (34.4%) or both (29.4%; p = .71), nor there were differences for CBR regarding the cumulative dose of the prior CAC. There was a trend towards a higher CBR in pts who received PLD >12 months versus $\leqslant$12 months since the end of their prior CAC (34.2 v 26.3%, respectively, p = .21) and in taxane naïve pts (39.4 vs. 27.7; p = .089). A significant association of PLD efficacy was detected for ECOG performance status (CBR 41%, 34%, and 14% in ECOG PS 0, 1, and 2, respectively; p = .006). This was reflected by a significantly longer progression-free and overall survival times for pts with ECOG 0 and 1 vs. 2 (both p < 0.001). In multivariate analyses and oligovariate adjustment models, results were maintained for ECOG performance status (p = .03 regarding CBR), but not for taxane pre-treatment and anthracycline-free interval, while they remained unchanged for the other parameters.
Conclusion: This meta-analysis demonstrates a significant CB from anthracycline rechallenge using PLD in pretreated MBC. The CBR was independent of resistance to, setting or total dose of, or time since previous conventional anthracycline therapy. A favorable ECOG performance status was the only independent predictive factor.

43LBA LATE BREAKING ABSTRACT

Combining genomic profiling (70-gene MammaPrint) with nodal status allows to classifypatients with primary breast cancer and positive lymph nodes (1–9) into very distinct prognostic subgroups that could help tailor treatment strategies.

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Objectives: The axillary lymph node (LN) status is considered to be one of the most important factors for chemotherapy decision-making of operable breast cancer patients (pts). It is commonly agreed that combination therapies with taxane-containing regimens should be recommended for these pts, whereas high-dose regimens have failed to provide further improvement for pts clinically considered at high-risk.
It has previously been shown that the 70-gene profile (MammaPrint®TM), which was developed in node-negative patients is excellent in predicting disease outcome in pts with 1–3 positive nodes and similarly in pts with 4–9 positive-nodes. Further analysis based on adjuvant treatment received and pooled analysis of the 2 LN positive series was performed in order to assess the prognostic added value of genomic profiling in LN positive pts.
Methods: Frozen tumor samples from breast cancer pts with positive LN coming from 2 hospitals were selected in consecutive series (1–3 LN, 4–9 LN; all female, diagnosed between 1984 and 1995, primary invasive breast carcinoma, unilateral T1, T2 or operable T3, mastectomy or breast-conserving therapy, no prior malignancies, fresh frozen tumor material available). Samples were evaluated by gene expression profiling for the 70-gene profile and were classified as genomic high risk (poor prognosis) or genomic low risk (good prognosis).
Results: A total of 519 pts have been analyzed: 346 with 1–3 positive LN (PN1) and 173 with 4–9 positive LN (PN2). Among them, 212 (41%) had the 70-gene good prognosis-profile and 307 (59%) had the 70-gene poor prognosis-profile (strictly equal proportions among the 2 LN groups). Median follow-up was 10.3 years: distant metastases occurred in 141 patients (116 as first event) and 103 (20) died of their disease. Distance metastases as first event and breast cancer specific survival according to LN group (PN) and genomic profile (MP) show the high prognostic value of genomic profiling in this patient population.
Conclusion: Our data show that the 70-gene profile is a strong prognostic marker of distant recurrence and breast specific death in breast cancer patients with positive LN. Combining nodal status (1–3 nodes vs. 4–9 nodes) and 70-gene profile (good vs. poor) allows stratifying patients among subgroups for whom tailored treatment strategies should be designed and assessed based on their very different outcome. Pts with elevated number of lymph nodes and high genomic risk have a very poor prognosis and might need to be considered for stronger treatment combinations.

44LBA LATE BREAKING ABSTRACT

Results of a phase I clinical trial of MGN1703, a novel TLR9-agonist, in patients with metastatic malignancies

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Background: The DNA-based immunomodulator MGN1703 stimulates the innate and cellular immune system mainly via the TLR9-receptor. The results of the recent *in vivo* experiments showed potent anti-tumor efficacy of MGN1703 in several mouse tumor models in prophylactic and therapeutic settings as well as a good safety profile in various animals. Two investigator-initiated pilot trials of MGN1703 as adjuvant in patients with metastatic solid tumors also showed good safety and tolerability of the drug as well as a positive effect on the response rate in patients treated with MGN1703.
Patients and Methods: In this phase I clinical trial MGN1703 is administered subcutaneously (s.c.) in escalating dosages (0.25 mg, 2 mg, 10 mg, 30 mg, and 60 mg; 3–6 patients per group) either in a single or in a multiple (2×/week over 6 weeks) dose regimen. Patients with metastatic tumors of the following entities are recruited for the study, if no other standard treatment options are available: Colorectal cancer, breast cancer,