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,

lung cancer, renal cell carcinoma and melanoma. Primary endpoints are to assess the safety and tolerability of escalating single doses and of escalating multiple doses of s.c. administered MGN1703, to determine the maximum tolerated dose (MTD) and dose limiting toxicity (DLT), and to recommend a dose for a phase II trial in patients.
Results: Currently, 12 patients have been treated and evaluated in the single dose groups of 0.25 mg, 2 mg, 10 mg and 30 mg (3 patients each). In the multiple dose group, 4 patients have been treated with 0.25 mg, 3 patients with 2 mg, 3 patients with 10 mg and 3 patients with 30 mg MGN1703, so far. Therapy was well tolerated except for sporadic transient symptoms like mild redness or induration of the injection site in 2 patients, increase of temperature to 38 degrees C in 1 patient, and mild fatigue in 2 patients. In the 0.25 mg group, 1 patient showed a SD after 6 weeks of treatment, and in the 2 mg group, 3 of 3 patients showed a SD after 6 weeks. Treatment results of the last 2 dosing groups are pending. The four responded patients were treated with MGN1703 for further 6 weeks within the extension phase of this clinical trial. Two of them had a SD after 12 weeks of treatment.
Conclusions: MGN1703 showed safety and tolerability at dosages up to 30 mg, so far. The detailed evaluation of clinical and immunological responses is still ongoing. There has been no DLT at this point of the Phase I trial.

45LBA LATE BREAKING ABSTRACT

Early results of randomized phase II trial of preoperative chemoradiotherapy or short-term radiotherapy for stage II and III rectal cancer followed by radical delayed (with 6 weeks interval) surgery

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Background: The mostly accepted preoperative treatment methods for locally advanced rectal cancer are concomitant chemoradiation (CTRT) followed by interval surgery or short term radiation (25 Gy, 5 fractions) (RT) followed by immediate surgery. There are no data from randomized trials regarding the effectiveness of short term radiation followed by delayed surgery. The aim of this study was to compare operative and pathological results after short-term radiotherapy or concomitant chemoradiotherapy followed by delayed surgery.
Material and Methods: 79 patients with stage II and III (resectable T3−4 N0 and T1−4N1−2) rectal adenocarcinoma were enrolled. 46 patients received concomitant chemoradiotherapy (50 Gy + 5-fluorouracil 400 mg/m2/d 1−4 d. on weeks 1 and 5 and leucovorine 20 LV mg/m2/d 1−4 d on weeks 1 and 5) and 33 received short-term radiotherapy (5 × 5 Gy). Surgery was performed 6 weeks after preoperative treatment in both groups. This study is still recruiting patients. Trial is registrated in website ClinicalTrials.gov, Identifier NCT 00597311.
Results: R0 resection rate was 91% in the CHRT group and 90% in the RT group ($p = 0.734$). Sphincter preservation rates were 67% vs 75% ($p = 0.578$) and postoperative complications rates were 26% vs 39% ($p = 0.326$) accordingly. There was no differences in postoperative pathological T and N stage, lymphatic and vascular invasion. Tumors were smaller after preoperative CTRT (2.4 cm vs 3 cm; $p = 0.04$). A mean of 9.7 lymph nodes per specimen were detected in the RT group and significantly fewer lymph nodes were detected in the CHRT group – 6.13 ($P = 0.001$).
Conclusions: Interim analysis of the trial data showed that preoperative chemoradiation resulted in statistically significant tumor downsizing comparing with short term radiation, but there were no difference in the rates of R0 resection and sphincter preservation between the two groups. Preoperative chemoradiotherapy resulted in fewer lymphnodes detected in the tumor-bearing specimen compared with short-term radiotherapy, with no differences in T and N stage.

46LBA LATE BREAKING ABSTRACT

15-years follow-up results of the randomized Dutch D1D2 Trial: lower cancer-related mortality after D2

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Background: A nationwide randomized clinical trial to study whether standardized D2 lymphadenectomy results in better survival rates compared with standardized D1 lymphadenectomy in patients with resectable gastric cancer, based on superior results after D2 lymphadenectomy in historical data and reports from Japan.

Material and Methods: Between August 1989 and July 1993, a total of 996 eligible patients were entered in the study. Of these patients, 711 (380 in the D1 group and 331 in the D2 group) underwent the randomly assigned treatment with curative intent and 285 underwent palliative treatment. At the time of the trial, resection of the spleen and pancreatic tail were regarded as necessary for adequate removal of D2 lymph node stations 10 and 11 in proximal tumors and in D1 in case of tumor invasion. Strict quality control measures for surgery and pathology were implemented and monitored. Data were collected prospectively and all patients were followed: Median follow-up for all eligible patients is 15.2 years (range, 6.9 to 17.9 years). This analysis focuses on the 711 patients treated with curative intent.
Results: Of the 711 patients treated with curative intent, one-hundred seventy four patients (25%) are still alive, all but one without recurrence. Overall 15-year survival rates for D1 and D2 are 22% and 28% respectively ($p = 0.35$). With 5-year survival rates of 45% and 47% and 11-year survival rates of 30% and 35% for D1 and D2 respectively, the results are the best recorded survival rates in Western countries.
Cause of death was further specified (see table below): gastric cancer related death rate was significantly higher in the D1 group compared with the D2 group, while death due to other diseases was similar in both groups. Local recurrence (22% in D1 vs. 12% in D2) and regional recurrence (19% in D1 vs. 13%in D2) was more frequent in patients after D1.

	Dissection		p-value
	D1 (n=380)	D2 (n=331)	
Cause of death			0.003
Alive	82 (22%)	92 (28%)	
Gastric cancer	182 (48%)	123 (37%)	
Other diseases	94 (25%)	77 (23%)	
Toxicity treatment	15 (4%)	32 (10%)	
Unknown	7 (2%)	7 (2%)	

Conclusions: Considering the superior cancer related death rates and recurrence patterns, and with a safer, spleen preserving D2 resection technique nowadays available in high volume centers, D2 is the recommended way to go in patients with resectable (curable) gastric cancer.
The outcome of the randomized Dutch D1D2 trial will change a D1 dissection as standard treatment into a D2 dissection for patients with gastric cancer as standard treatment in daily practice.

47LBA LATE BREAKING ABSTRACT

Phase II trial of sorafenib with capecitabine and oxaliplatin (SECOX) in patients with locally advanced or metastatic hepatocellular carcinoma

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Background: This is a single arm, multi-centre, phase II study to assess the efficacy and tolerability of sorafenib combining oxaliplatin and capecitabine for the treatment of advanced hepatocellular carcinoma (HCC) patients.
Methods: Advanced HCC patients with no prior systemic therapy received SECOX regime – sorafenib 400 mg bid (Day 1−14), oxaliplatin 85 mg/m^2 (Day 1) and capecitabine 1700 mg/m^2 (Day 1−7) every two weeks. Response assessment using RECIST criteria was performed after 4 cycles. Patients who achieved partial response or stable disease would receive another 4 cycles till a maximum of 8 cycles. Afterwards, sorafenib was continued till disease progression. The primary endpoint was time-to-progression (TTP) and the secondary endpoints were tumor response rate (RR), overall survival (OS) and tolerability.
Results: A total of 51 patients were enrolled in the trial. The median age was 58 years (range, 28−81) and all patients were in ECOG Performance Status 0−1. Eighty-four percent of patients were chronic hepatitis B carriers and 98% of patients had Child A cirrhosis. Ten (20%) patients had tumor vascular invasion and 41 (80%) patients had extra-hepatic metastasis. The best RR was 14 % and another 61% of patients achieved stable disease. Overall, 75% of patients derived clinical benefits from SECOX regime for at least 8 weeks. The median TTP was 7.1 months (1.7–19.9) and OS was 10.2 months (2.1–20.5). Hand-Foot-Skin reaction (73%), diarrhea (69%) and neutropenia (63%) were the most commonly encountered toxicities,