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,

with the majority of patients having grade 1 or 2 toxicity. No treatment-related death was reported.
Conclusion: The SECOX regime demonstrates highly significant clinical activity and good tolerability in advanced HCC patients. Our data support a randomized trial comparing SECOX versus Sorafenib alone for treatment of advanced HCC.

48LBA LATE BREAKING ABSTRACT
Algorithmic classifiers to diagnose bladder cancer

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Background: Algorithmic classifiers with high diagnostic accuracy have the potential to reduce expensive diagnostic and monitoring investigations in bladder cancer.
Methods and Patients: A case control trial sponsored by Randox Laboratories Ltd, Northern Ireland, recruited 161 patients aged between 19 and 84, with a history of haematuria who had undergone cystoscopy. Seventy-seven (55 males; 22 females) had negative urethroscopy and/or pathology and 84 (69 males; 15 females) had pathologically proven bladder cancer ($\leqslant$pT1G2, n = 53; $\geqslant$pT1G3, n = 31). Our objective was to establish proof of concept that multivariate diagnostic algorithms could achieve more accuracy to diagnose bladder cancer, than single biomarkers. Following consent, 10 ml of blood and $\geqslant$100 ml of urine were collected. Urine analyses included nuclear matrix protein 22 (NMP22), cytology, protein creatinine and osmolality. Carcinoembryonic antigen (CEA) and free Prostate Specific Antigen (FPSA) and total PSA (TPSA) were assessed on serum. Detailed demographics, medical histories and investigation results were recorded.
Results: Bladder cancer patients smoked more and for longer and had significantly higher urinary protein levels than controls. Bladder Tumour Antigen (BTA), CEA, D-Dimer, Epidermal Growth factor (EGF), Fas, FPSA, interleukin (IL)-1α, IL-2, IL-6, IL-8, Matrix Metalloproteinase-9 (MMP-9), MMP-9/Neutrophil-associated Gelatinase Lipocalin (NGAL) and Vascular Endothelial Growth factor (VEGF) levels were significantly higher in bladder cancer patients and C-Reactive protein (CRP) and EGF were significantly higher in controls ($p < 0.05$; t-test). The sensitivities and specificities of individual markers ranged from 33 to 68% and 52 to 95%, respectively. NMP22 and cytology had sensitivities of 58% and 33% and specificities of 87% and 95%, respectively. Nine algorithmic classifiers created using logistic regression analyses, included CEA, D-Dimer, EGF, IL-2, monocyte chemoattractant protein-1 (MCP-1), Neuron Specific Enolase (NSE), NMP22, Thrombomodulin (TM), VEGF and von Willebrand factor together with smoking years and whether or not patients were taking anti-hypertensive medication. Sensitivities of these algorithms ranged from 73 to 88% and specificities from 72 to 81%.
Conclusions: These findings have established proof of concept of multivariate algorithmic classifiers for bladder cancer. This is the first time that anti-hypertensive medication has been associated with diagnosis of bladder cancer.

49LBA LATE BREAKING ABSTRACT
Final results of a Phase II randomised study of cediranib (RECENTIN™) in patients with advanced renal cell carcinoma (RCC)

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Background: Cediranib is a highly potent VEGF signalling inhibitor of all three VEGFRs suitable for once-daily oral dosing. This Phase II, randomised, double-blind, parallel-group study (study code 2171IL030) compared the efficacy of cediranib with placebo (P) in patients with metastatic or recurrent RCC.
Materials and Methods: Patients were randomised 3:1 to cediranib 45 mg/day or P. The primary objective was to determine the efficacy of cediranib by comparing changes in tumour size after 12 weeks of therapy. Secondary objectives included assessments of response rate and duration (RECIST), progression-free survival (PFS), and safety/tolerability. After 12 weeks (or upon progression if earlier), treatment was unblinded and patients on P were given the option of receiving cediranib.
Results: Seventy-one patients were randomised (cediranib, 53; P, 18). After 12 weeks, there was a highly significant difference in mean % change from baseline in tumour size between cediranib (−20%) and P (+19%; $P < 0.0001$); 14/18 P patients went on to receive cediranib. At data cut-off, the mean best change in tumour size was −31% for cediranib; 10/14 P patients who later received cediranib had a subsequent reduction in tumour size. In the cediranib arm, 18 patients (34%) achieved a partial response (PR; 12/18 still had a PR at data cut-off, 9 for $\geqslant$1 year), and 25 patients (47%) experienced stable disease (disease control rate, 81%). The cediranib arm showed a significant prolongation in PFS vs the P arm, which included P patients who later received cediranib (hazard ratio [HR] = 0.45 [90% CI 0.26, 0.78]; $P = 0.017$); median PFS was 12.1 and 2.7 months for the cediranib and P arms, respectively. If all patients who received a different cancer therapy to their randomised treatment were censored at the time of switching therapy, the HR was 0.14 (90% CI 0.06, 0.30; $P < 0.001$). The most common adverse events (AEs) with cediranib were diarrhoea (59; 88%), fatigue (44; 66%), dysphonia (42; 63%) and hypertension (41; 61%). The most frequent CTCAEs grade $\geqslant$3 were fatigue (13; 19%), hypertension (13; 19%) and diarrhoea (9; 13%). A total of 58 patients (87%) receiving cediranib had a dose reduction or pause, with a median time to first reduction or pause of 29 days; the mean dose was ~30 mg/day.
Conclusions: In this study of patients with advanced RCC, cediranib monotherapy showed significant evidence of clinical benefit with an AE profile that was generally consistent with previous studies with cediranib 45 mg.

50LBA LATE BREAKING ABSTRACT
Radical hysterectomy for small cervical cancer: role of robot assisted laparoscopy

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Objective: The aim of this study is to demonstrate the feasibility and the interest of robotic-assisted laparoscopic radical hysterectomy with pelvic lymphadenectomy in early cervical cancer – tumor size less than four centimeter − in comparison to a series of patients managed by conventional laparoscopy in our 2 institutions.
Study design: We compared our series of 14 first patients with prospective data collection operated on by experimented laparoscopic surgeons with the Da Vinci surgical system with 14 patients with previous or contemporary laparoscopic surgery. We studied surgical time, estimated blood loss, length of stay, lymph node yields, residual cervical tumor, parametrial invasion and complications.
Results: There was no statistically difference between the 2 groups in term of body mass index, age, FIGO stage and previous brachytherapy.
Compared with laparoscopic surgery, robotic surgery had a longer operative time (263 vs 200 minutes, $p < 0.005$) and a shorter length of stay (3.7 vs 5.6 days, $p < 0.005$).
There was a tendance to less post operative complications in the robotic group compared in the laparoscopic group (7.1 vs 57.1%, NS) with less urinary complications (0% vs 28.6%, NS). No difference was found in regards to estimated blood loss (57 vs 89 mL, NS) and parametrial invasion and lymph node yields (16.8 vs 19.9, NS).
Conclusion: Robotic-assisted laparoscopy is feasible in case of small cervical cancer. This new surgical approach is comparable to laparoscopy and is an other offer of minimally invasive surgery.