various malignancies, its role in gallbladder carcinoma (GBC) remains undiscovered.
Methods: We studied SDF-1α protein expression in 72 specimens of GBC using immunohistochemistry, and analyzed the clinicopathological features and clinical outcomes. GBC cell lines, SNU-308 and JCRB1033, were studied *in vitro* and *in vivo*. Specific depletion or overexpression of CXCR4, which is a receptor for SDF-1α, in GBC cell lines was achieved by expression of a small interfering RNA (siRNA) against CXCR4 and lentivirus-mediated transduction, respectively.
Results: We observed the constitutive expression of SDF-1α in patients with gallbladder carcinoma (GBC) and recognized inverse correlation between the level of SDF-1α expression and their overall survival. In addition, SDF-1α expression was significantly associated with high histologic grade and lymph node involvement. Multivariate analyses showed that SDF-1α expression (HR, 8.252; 95% CI, 1.116–61.043; $P = 0.039$) and lymphatic invasion (HR, 10.346; 95% CI, 1.304–82.080; $P = 0.027$) were independent risk factors for overall survival. Furthermore, we demonstrated functional involvement of SDF-1α and its receptor CXCR4 in the growth, motility, invasiveness, and adhesiveness of GBC cells. Stable depletion of CXCR4 even with SDF-1α stimulation led to a significant decrease in GBC cell proliferation, migration, and invasion while overexpression of CXCR4 with SDF-1α stimulation showed enhanced these cellular activities and increased intracellular signaling through ERK, AKT and FAK. In a GBC xenograft nude mouse model, SDF-1α overexpression stimulated tumorigenicity of GBC cells.
Conclusions: These results indicate that GBC cells express both SDF-1α and its receptor by tumour itself and SDF-1α may have a role in GBC progression through an autocrine mechanism. Thus, targeting SDF-1α and its receptors may provide a novel therapeutic strategy for GBC treatment.

6513 POSTER

Reporting Patient Characteristics and Stratification Factors in Randomized Trials of Systemic Chemotherapy for Advanced Gastric Cancer

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Background: There is no consensus on what patient characteristics are most suitable to report or be used as stratification factors in clinical trials for advanced gastric cancer (AGC), to our knowledge.
Patients and Methods: We conducted a comprehensive review of published randomized trials for AGC to examine the patient characteristics that were reported.
Results: Among the 67 analyzed trials, age, gender, performance status, proportion of measurable disease, and previous gastrectomy were frequently reported (>69%). Histology, number of disease sites, and adjuvant treatment were reported in less than 50% of trials. Although the reporting of second-line chemotherapy has increased in recent trials, it remains at less than 50%. Notably, recent trials have tended to include patients with better performance status and less locally advanced disease, with Asian trials more frequently including patients with more diffuse histology and less locally advanced disease or liver metastasis than non-Asian trials. Stratification was conducted in approximately 60% of trials using quite variable stratifying factors.
Conclusion: Inconsistency exists in the reporting of patient characteristics, the characteristics themselves, and use of stratification factors in clinical trials for AGC. A consensus set of important patient characteristics and strata may be necessary to conduct and interpret quality, randomized studies.

6514 POSTER

Genetic Polymorphism of IGF1 Predicts Recurrence in Patients With Gastric Cancer Who Have Undergone Curative Gastrectomy

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Background: To our knowledge, no reports have evaluated the effects of genetic polymorphisms of IGF1 on clinical outcomes of gastric cancer patients.
Methods: We retrospectively analyzed the impact of IGF1 polymorphisms on recurrence-free survival (RFS) in 430 patients with gastric cancer who underwent curative gastrectomy between 2001 and 2005 in our institution.
Results: Among the 430 gastric cancer patients, 345 were pathological stage I or II, while 85 were stage III or IV. The median 5-year RFS rate was 85.3% (95% confidence interval, 81.4–88.5). In a multivariate Cox model (adjusted for age, gender, histology, pathological stage, adjuvant chemotherapy, and history of diabetes), two IGF1 polymorphisms, rs1520220 and rs2195239, were significantly associated with RFS (HR 0.60, 95% CI, 0.40–0.91; and HR 0.60, 95% CI, 0.41–0.89, respectively, in a per-allele model). When stratified by stage (I-II vs. III-IV), rs1520220 in particular was associated with RFS in patients with stage III-IV disease, with a P value for interaction of 0.01.
Conclusion: Our findings indicate that genetic polymorphisms of IGF1 may have a substantial effect on recurrence for gastric cancer patients who have undergone curative gastrectomy. This information may help identify population subgroups that could benefit from IGF-1 targeting agents.

6515 POSTER

Application of the Trifunctional Antibody Catumaxomab as Part of a Multimodal Approach in Resectable Gastric Cancer is Feasible and Promotes the Development of Tumour-specific Immune Responses

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Background: Although perioperative chemotherapy (CT) is beneficial in gastric cancer (GC), a significant number of patients will eventually relapse. The trifunctional antibody (Ab) catumaxomab targets (1) the epithelial cell adhesion molecule (EpCAM) on malignant cells, (2) CD3 on T cells, and (3) triggers Ag-presenting cells via their Fcγ-receptor. While catumaxomab has been approved for the treatment of malignant ascites, it has not been investigated in a perioperative setting and the immune mechanisms behind its clinical effects have not conclusively been elucidated.
Methods: In a phase II study, patients with operable GC received neoadjuvant platinum-based CT followed by 10 μg of catumaxomab intraoperatively and 4 consecutive doses (10–20–50–150 μg) applied intraperitoneally in the adjuvant setting. Primary safety endpoint was the rate of predefined postoperative complications. Efficacy endpoints included disease-free (DFS) and overall survival. The immunomodulatory effect of catumaxomab was investigated before surgery, after application of the first dose, and 1 month post treatment.
Results: 54 patients completed ⩾1 cycle of CT, surgery and ⩾1 catumaxomab dose. Most of these patients (N = 30; 56%) received all five catumaxomab infusions. The primary endpoint was met as predefined postoperative complications were reported for only 18 patients (33%; 95% CI: 21−48%) which was below the predefined maximum tolerable rate of 62%. Most frequent complications were pulmonary infection, anastomosis insufficiency and abscess. Immunomonitoring of 6 selected patients revealed a transient decrease in peripheral CD4+ T cells with an effector and T-helper (Th)-1 phenotype directly after Ab application. All patients investigated evidenced pre-existing EpCAM-specific CD4+ and/or CD8+ T cells. While these T cells disappeared from the peripheral blood (PB) immediately after Ab exposure, we detected increased numbers of peripheral EpCAM-specific cells 4 weeks after catumaxomab treatment. During a 1-year follow-up, 13/49 evaluable pts (27%) relapsed, 2 of whom died. DFS was 74% (95% CI: 61−86%).
Conclusions: Catumaxomab as part of a multimodal therapy is a feasible option for primarily resectable GC. The 1-year follow-up efficacy data suggest a beneficial effect on DFS. Catumaxomab might exert its clinical effects i.e. by causing a redistribution of effector and Th1-type cells from the PB into peripheral tissues and expanding pre-existing EpCAM-specific T cells.

6516 POSTER

Management of Stage 4 Metastatic Neuroendocrine Disease − Outcomes and Cost-effectiveness

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Background: Management of hepatic neuroendocrine metastases remains controversial. Surgery with curative intent aims to resect all pre-operatively identifiable disease, whilst cytoreductive surgery for symptom control is appropriate when 90% of tumour burden can be removed. Radiological and symptomatic recurrence rates remain high. This study aimed to

assess whether surgical intent (curative or cytoreductive) has an impact on long-term outcome, and assess cost-effectiveness of surgery for the symptomatic management of hepatic neuroendocrine metastases.
Methods: A retrospective review of a prospectively maintained database of all patients referred to a neuroendocrine multidisciplinary team meeting between January 1996 and December 2008.
Result: 340 patients were referred during the study period, of whom 190 (55.8%) had disease stage 1−3. Of the remaining 150 patients with stage 4 disease, 117 (78%) were treated non-surgically (6 RFA, 15 MIBG, 51 octreotide, 23 lantreotide, 2 dotate, 2 chemoembolisation) whilst 33 patients (22%) were treated by surgical resection. Thirteen underwent surgery with curative intent, whilst 19 underwent cytoreductive resection. At median follow-up of 66 months, 8 of the 13 patients (62%) who underwent curative resection had hepatic recurrence. Overall 1, 3, and 5-year survival rates were 94%, 64% and 46% for stage 4 medically medically managed patients, 100%, 100% and 82% for patients undergoing cytoreductive surgery and 100%, 100%, 100% for patients undergoing curative resection. (p = 0.049). Curative resection gave a median duration of symptom control of 67.5 months (IQR 36.5−81) compared to 24 months (IQR 19–45.5) for cytoreductive surgery. Cost per QALY for the treatment of hepatic neuroendocrine metastases was €1,438 for curative surgery and €3,121 for cytoreductive surgery, compared to €14,450 for non-surgical management.
Conclusions: Hepatic resection improves survival in patients with neuroendocrine metastases. Although recurrence rates are high, curative surgery is associated with more durable symptom control than cytoreduction. Resection for symptom control is considerably more cost-effective than medical management.

6517 POSTER

Sunitinib and Transarterial Chemoembolization (TACE) for Advanced Hepatocellular Carcinoma (HCC)- Final Results of a Phase 2 Trial

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Background: TACE and oral anti-angiogenic agents have individually been effective for treating inoperable HCC. We evaluated the effects of a combination of sunitinib and TACE on PFS in this prospective phase 2 study.
Methods: Eligibility: PS 0, 1, inoperable HCC, Child Pugh A or B, platelets >100K, bilirubin 2 or less and no contraindication to TACE. Treatment: Cycle (C)1-Sunitinib 37.5 mg po day (d)1−7 followed by TACE with doxorubicin in lipodiol on d8, continued sunitinib 37.5 mg po qd d15−36 followed by 2 weeks off. C2 onwards- sunitinib 4 weeks on and 2 weeks off, with dose escalation to 50 mg in patients (pts) without any grade 3 toxicities in C1. DCE MRI, sVEGFr, monocytes, and sunitinib PK were assessed at baseline, d 8, 10 and 36.
Results: Baseline characteristics of 16 pts were following: median age 74 years (range 40−86), 12 males and 4 females, all with Child Pugh Class A cirrhosis (etiology: hepB: 2, hepC: 6, alcoholic: 1, unknown: 7), and ECOG PS 0: 12 and PS 1: 4. There were 10 liver only and 6 extrahepatic disease sites. Median PFS was 8 mo (95% CI 4.3−9.3) and OS was 14.9 mo (95% CI 6.3–27.1) with a median follow up of 12.8 months, and 5 patients still alive. Responses by RECIST criteria were 2 PR,11 SD, and 3 clinical deteriorations; clinical benefit rate was 81%. Median number of cycles on study was 3 (range 1−7). For 8 pts with DCE- MRIs, median Ktrans change was −20% after 7 days of sunitinib and a 7% further decrease was seen after TACE and sunitinib; decrease in viable tumour at same timepoints was 3% (d8) and 15% (d36) respectively. Steady-state sunitinib concentrations ranged from 20–150 ng/mL, which were above the IC_{50} values of 4−30 ng/mL for VEGF inhibition. PK/PD modeling estimated sunitinib IC_{50} values of 15 and 10 ng/mL for modulation of Ktrans and AUC_{90}. sVEGFR2 levels increased with Ktrans and AUC_{90}. Median monocyte counts were 0.4 x 10 x9/L before and decreased by 50% on d36 after TACE. Eleven pts (69%) had grade 3/4 toxicities attributable to sunitinib. Of the 57 total events, the most frequent (n = 5 or more) were thrombocytopenia (10), amylase/lipase increase (9), lymphopenia (7) and fatigue (6). Dose delays and dose reductions occurred in 13 and 3 patients respectively. Reasons for discontinuing therapy were toxicity (7), progression of disease (7) and withdrawal of consent (2).
Conclusions: This is the first study of sunitinib and TACE in HCC. Improvement in PFS and OS was seen with acceptable toxicity. Our studies show a relationship between sunitinib concentration and following markers: Ktrans, AUC_{90}, $sVEGFR_2$ and monocytes, with additional decrease seen after TACE.

6518 POSTER

Neoadjuvant Chemoradiotherapy for Locally Advanced Esophageal Cancer − Analysis of Pattern of Recurrence and Prognostic Factors for Survival

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Background: Concurrent chemoradiotherapy (CRT) followed by esophagectomy has become a standard treatment option in patients with resectable esophageal cancer. We analyzed pattern of recurrence and factors predictive for survival to find additional strategies to improve outcome.
Material and Methods: Between 2003 and 2009, 64 patients were treated with neoadjuvant chemoradiation followed by surgery as a planned approach for locally advanced esophageal cancer in our institute. All demonstrated a clinical T-stage of 2 or higher and histology was squamous cell carcinoma in all patients. The average age was 62.1 years, and most patients were male (89%). 14 patients (22%) had cStage II, 41 (64%) had cStage III and 9 (14%) had cStage IVa carcinomas (UICC-TNM 6th). A total of 36 patients received a combination of docetaxel and 5-Fluorouracil (5-FU) while 27 patients received a combination of cisplatin and 5-FU, and one received a combination of nedaplatin and 5-FU. The radiation was administered concomitantly and total dose was 40 Gy. Surgical resection was performed 4−6 weeks after the completion of chemoradiotherapy, using a right transthoracic approach with two- or three-field lymph node dissections.
Results: The overall clinical response rate to neoadjuvant CRT was 93.8%; 9 showed complete response (CR), 51 showed partial response (PR). On examination of the resected specimens, pathological CR was achieved in 16 patients (25%). Another 22 patients (34%) had a significant tumour response with only minimal tumour remaining. According to the clinical stage before CRT, 5-year survival was 75% in cStage II, 45% in cStage III and 27% in cStage IVa. Among 44 patients who were followed-up beyond 2 years, 22 patients experienced disease progression. Of the treatment failures, 8 (18% of 44 patients) were distant, 8 (18%) were locoregional, and 6 (14%) were both locoregional and distant failure. In patients who achieved pathological response, 2 courses of additional chemotherapy after surgery prolonged survival compared to patients without postoperative chemotherapy (p < 0.001), while no difference was seen in patients who had no pathological response. By multivariate analysis clinical response to neoadjuvant CRT (HR 0.09; p = 0.0003) and pathologic response (HR 4.17; p = 0.001) were factors predictive of overall survival.
Conclusions: As compared with our previous data of treatment failures in patients who underwent surgery alone, locoregional recurrence rate decreased, while distant recurrence rate did not change. Control of distant recurrence is considered to be the most important problem. In multivariate analysis, clinical and pathological response to neoadjuvant CRT were significant predictor of survival. Therefore, new CRT protocol that affects both locally and systemically including multi-agent chemotherapy or molecular targeting drugs should be needed to improve survival.

6519 POSTER

Role of Surgical Resection in Complete Responders on FDG-PET After Chemoradiotherapy for the Locally Advanced Esophageal Cancer

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Background: Trimodality therapy has been a standard treatment for locally advanced esophageal cancer, and definitive chemoradiotherapy (CRT) is an alternative treatment for unresectable or medically inoperable cases. But in patients who have a good response to CRT, the role of surgical resection is not clearly verified. The purpose of this study is to determine the prognostic significance of metabolic response and what the role of surgery is in complete responders on [^{18}F]Fluorodeoxyglucose positron emission tomography (FDG-PET) after CRT for locally advanced esophageal cancer.
Material and Methods: We retrospectively reviewed 162 patients with locally advanced esophageal cancer with increased uptake on FDG-PET before chemoradiotherapy. Of these, 89 patients received definitive CRT and 73 patients received surgery after preoperative CRT. FDG-PET was repeated 1 month after CRT, and metabolic complete remission (PET-CR) was defined as standard uptake value (SUV) of 3 or less. Overall survival (OS), disease free survival (DFS) and local recurrence free survival (LRFS) rates were compared between the two groups.