and adequate organ function. Irinotecan (150 mg/m^2) was given on first day, repeated every 2 weeks in irinotecan monotherapy group (arm A), and irinotecan (150 mg/m^2) was given on first day with leucovorin (folinic acid) (20 mg/m^2) followed by 5-FU (2000 mg/m^2 continuous infusion over 48 hours), repeated every 2 weeks in irinotecan plus 5-fluorouracil/leucovorin combination group (arm B). Response was assessed every 4 cycles by computed tomography. The primary end point was response rate and time to treatment failure.
Results: Between March 2007 and February 2009, 36 eligible patients entered. In Arm A, 17patients were evaluable for objective response and 18 patients for safety. In Arm B, 16 patients were evaluable for objective response and 18 patients for safety. The median age was 60 years and the median follow up duration for surviving patients was 9.4 months. Disease status was comparable for both arms. 3 of 17 (17.6%) patients had a confirmed objective response in arm A (95% confidence interval [CI] 0.07−28.2%) and 3 of 16 (18.7%) patients had a confirmed objective response in arm B (95% CI 0−0.37%). No significant difference was noted between the arms both for ORR (p = 0.642) and for disease control (29.4% vs. 37.5%, respectively, p = 0.91). Progression free survival time was 2.9 months vs. 3.0 months (p = 0.677), median overall survival was 4.6 months (95% CI 2.56−6.68%) vs. 7.6 months (95% CI 1.79−13.4%) in arm A and B, respectively (p = 0.145). There was no relevant difference in the occurrence of overall grade 3/4 toxicity between the two arms. Neutropenia was the most common grade 3/4 toxicity (50.0% vs. 62.1%, respectively). There was one thromboembolic event in arm A.
Conclusions: The preliminary results showed that both treatment arms have similar clinical efficacy as salvage treatment in advanced/metastatic gastric cancer. But irinotecan plus 5-fluorouracil/leucovorin combination group has a tendency of longer overall survival time. Each regimen has a manageable tolerability profile. The accrual is ongoing.

6579 POSTER

Cetuximab with Irinotecan/Folinic Acid/5-FU as first-line treatment in advanced gastric cancer: a prospective multi-center phase II study and additional biomarkers of the Arbeitsgemeinschaft Internistische Onkologie

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Background: Cetuximab combined with irinotecan/folinic acid/5-FU (IF) based therapies demonstrated high efficacy in human metastatic colorectal cancer. In advanced gastric cancer, IF may be an effective and well tolerated alternative to cisplatin-based regimens. We therefore conducted a phase II AIO study to evaluate the tolerability and efficacy of cetuximab with IF as first-line treatment in patients (pts) with advanced gastric cancer. In parallel, we analysed mutation status of KRAS, BRAF, PIK3CA and levels of lymphangiogenic ligands VEGF-C, VEGF-D and VEGFR3.
Methods: Pts were eligible with previously untreated adenocarcinoma of the stomach or oesophagogastric junction, ECOG performance (PS) < 2, measurable lesions and adequate organ functions. Pts received weekly cetuximab (first 400, subsequently 250 mg/m^2) combined with chemotherapy of irinotecan (80 mg/m^2) + 24 hour continuous infusion of sodium folinic acid (Na-FA: 200 mg/m^2) and 5-FU (1500 mg/m^2) on days 1, 8, 15, 22, 29, 36 of a 50-day cycle. Treatment was continued until tumor progression and assessments were performed every 2nd cycle. KRAS; BRAF, PIK3CA, VEGFR3, VEGF-C, VEGF-D analysed by PCR, sequencing, ELISA or immunohistochemistry (IHC) in tumor blocks and serum samples were correlated with stage, response and survival.
Results: From Aug 2006 – Sep 2007, 49 pts were enrolled: 71% were males, median age was 63 years (33−77), median PS was 0 (65% pts), 69% and 31% of pts had gastric and esophagogastric junction carcinomas, respectively. Median treatment duration was 15.2 weeks (range 1.1−69.1). Grade 3/4 toxicities were diarrhoea (17%), skin reactions (13%), anorexia (9%), anaemia and fatigue (7%), allergic reactions, neutropenia (4% each). Among 48 pts evaluable for response, overall response rate (CR + PR) was 42% (CR 4%/PR 38%) and tumour control rate was 73%. Median progression-free and overall survival times were 8.5 months (36.6 weeks; 95% CI 30.1; 48.1) and 16.6 months (71.1 weeks; 95% CI 50; 93.4), respectively. Translational tests of 38 pts significantly correlated IHC expression levels of VEGF-C (p = 0.03) and VEGF-D (p = 0.025) with incidence of metastases. Low VEGF-C correlated with response (p = 0.041), low VEGF-D hd a trend to better survival (p = 0.052).
Conclusion: Cetuximab plus IF was well tolerated and encouraging survival data were observed. Further biomarkers will be analysed and presented at the meeting. Currently, cetuximab combined with chemotherapy in advanced gastric cancer is under further investigation in an ongoing phase III trial.

6580 POSTER

S-1 combined with weekly cisplatin for metastatic gastric cancer

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Background: The investigators of the recent phase III SPIRITS trial found that the addition of cisplatin to S-1 provided a significant overall survival advantage over treatment with S-1 alone. However, this treatment regimen required a short-term hospital stay for hydration to prevent the renal toxicity induced by cisplatin, and this therefore negates the convenience of using an orally administered drug such as S-1.
Several phase I or II studies showed the efficacy and safety of S-1 combined with weekly cisplatin therapy for advanced and recurrent gastric cancer. To evaluate the efficacy of weekly intravenous (i.v.) cisplatin and S-1 combination therapy for patients with metastatic gastric cancer, we retrospectively examined 46 patients with advanced gastric cancer previously untreated.
Materials and Methods: The participants were 46 patients treated at our hospital. S-1 at 80 mg/m^2 daily was administered orally in two divided doses for 2 weeks, followed by a 2-weeks rest. Cisplatin at 30 mg/m^2 was administered by intravenous drip infusion over 90 minutes with a minimum prehydration of 500 ml normal saline, including granisetron, on days 1 and 8. This treatment was repeated every 4 weeks (one cycle each) until disease progression or unacceptable toxicity was seen.
Results: A total of 212 cycles were administered, with a median of five cycles (range: 1−14) per patient. The results were rated as a complete response in 3 cases, partial response in 19 cases and stable disease in 12 cases. The response rate was 47.8% (22/46) and the median survival time was 16.0 months. The one-year survival rate was 67.0%. The major adverse reactions were myelosuppression and gastrointestinal symptoms.
Conclusions: The combination of S-1 and weekly cisplatin therapy appears to be highly efficacious and safe and shows promise as a useful treatment strategy, even in outpatient clinics.

6581 POSTER

Von willebrand factor and fibrinogen levels predict outcome in advanced gastric cancer patients

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Background: Activation of clotting and fibrinolysis systems are thought to be involved in tumor angiogenesis, tumor-platelet adhesion and tumor-endothelial cell adhesion. Von Willebrand factor (vWf), an adhesive ligand with platelets, is elevated in advanced disseminated malignancies and it is involved in the metastatic process.
Objective: To correlate coagulation markers levels in plasma of advanced gastric cancer (GC) patients (pts) undergoing palliative chemotherapy (CMT) with response to treatment and time to progression (TTP).
Materials and Methods: 41 pts with locally advanced or metastatic GC, diagnosed between january and december 2008, and 20 healthy controls were enrolled in the study. Blood samples were taken before (basal time) and after platinum-fluoropirimidine-based CMT. We measured plasma levels of vWf, vWf activity-ristocetin cofactor test (vWf: Rcof) (BCS coagulometer), vWf Antigen (vWf:Ag), factor VIII activity test, D-Dimer (DD), Plasminogen, Thrombin Time (TT), Fibrinogen and Reptilase time (ACL-TOP coagulometer) and plasma GC tumor markers (CEA and CA19.9).
Results: Median age of pts was 64 (range 38−89). All pts but one received at least one cycle of CMT, with a median of 3 cycles (range 0−10). Median basal ECOG was 1 (range 0−3). After a median follow-up of 9 months the median TTP was 4 months and the median overall survival (OS) 8 months. At basal time were found elevated levels of vWf:Ag (median 210%; range 121.1–492.2%), DD (median 530 gr/L; range 49–17489) and Fibrinogen (median 5.4 gr/L; range 2.78−7.67) when compared with healthy controls. Basal time plasma levels of vWf:Ag were significantly correlated with basal CA19.9 levels (p < 0.05). Higher basal Fibrinogen levels predicted worse response to treatment (p = 0.02) and shorter TTP (p = 0.012); however basal time levels of vWf:Ag and DD were not correlated with CMT response, TTP or OS. Higher vWf:Rcof levels after 3 cycles of CMT were correlated with worse treatment response (p = 0.019) and shorter TTP (p < 0.05).

Conclusions: vWF:Rcof levels during CMT and basal levels of Fibrinogen might both predict response to treatment and TTP in advanced GC pts.

6582 POSTER

Long-term results of surgical treatment of recurrent gastric cancer

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Background: To improve the treatment effect of recurrent gastric cancer by using repeated surgical procedures.
Materials and Methods: 82 patients with recurrent gastric cancer operated because of antral zone cancer in general surgery and oncological hospitals have been made over 2000 to 2008. The patients aged from 24 until 76 years old. Men prevailed 65 (79.3%), women 17 (20.7%). Patients operated were divided into 2 groups: 1-st consisted of 33 (40.2%) patients operated in volume of distal subtotal resection by Billrot-I, 2-nd consisted of 49 (59.8%) patients operated in volume by Billrot-II. In 1-st group relapse-free time was 6.1±0.3 mth, in 2nd – 12.8±0.2 mth. Morphological structure of 29% tumour observations were presented high and moderate differentiated adenocarcinoma, in 71% – low-grade differentiated adenocarcinoma. In all 82 cases lymphodissection corresponed to volume D1, and just in 24 cases to volume D2. By growth form infiltrative form 44 (53.7%) was the most occurred, endophytic form was in 27 (32.9%) cases, and in exophytic form was in 11 (3.4%) cases. Tumour localized in antral zone in 14 (17.1%) patients, 39 (47.6%) in antral zone transiting on lower third gastric body, 29 (35.3%) in antral zone with transition on middle third gastric body. Of 82 patients only 36 (43.8%) ones were performed repeated operative procedures, 23 (63.8%) of them were made radical surgery. 12 (52.2%) of them were made combined surgery. If unresectable, considering stenosis of gastroenteroanastomosis 10 (27.8%) patients were made draining surgery. In 3 (8.3%) cases because of spread of tumour process explorative laparatomy was performed.
Results: Frequency of complications after recurrent cancer gastric surgery being 19.4%, lethality 8.3% (3 patients). The most highest respectability was 66.7% after gastric resection by Billrot-II, after resection by Billrot-I – 33.3%. After radical surgery the median of survival rate in groups was: in 1 group 14.2±0.7 mth, and in 2 group 22.3±0.6 mth.
Conclusions: Resectability by Billrot-I surgery was twice less than by Billrot-II. Relapse-free time is twice less than in Billrot-II. Experience showed that there is the need to develop the principles of early diagnostics to improve the radical surgery results for patient with recurrent gastric cancer.

6583 POSTER

Ways of optimization of principle splenectomy in extensive gasterectomy

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Background: to work out modern approaches to principal splenectomy performance in surgical treatment of gastric cancer.
Materials and Methods: there made comparative analysis of direct results of surgical treatment of 137 patents with gastric cancer over 2000–2007. Patients were divided in 2 groups: 1) patients subjected extensive gasterectomy in volume D2 with splenectomy and resection of tail part of pancreas (n = 70), 2) subjected to extensive gasterectomy in volume D2 with preservation of pancreas (n = 67). As known intensity and direction of metastasis in lymph nodes, identify the properties of initial tumor invasion, localization, form growth, histological structure. To identify the need of removal 10 groups of lymph nodes we studied the frequency of damage of these group lymph nodes depending on different prognostic factors.
Results: when analyzed 70 extensive gasterectomy metastasis damage of regional lymph nodes (N+) revealed in 68 (9.2%) cases. From them the metastasis of operated patients were in N1–100%, N2−91.4%. In morphological study of 10 groups of lymph nodes metastasis were revealed in 28.5%. Metastatic damage of pancreas reported in 2.8% cases. Metastasis analysis in lymph nodes of pancreas portal in the depending on tumor localization showed that in 45.0% (9/20) cases of metastasis noted in proximal part of stomach cancer, in 25.0% (5/20) cases in stomach tumor and in 30.0% (6/20) in total stomach affection. Metastasis in lymph nodes of pancreas portal was not observed in affection of antral zone of stomach. No metastases were in 10th group of lymph nodes in exophytic form growth. The more frequent metastatic process was revealed in diffuse type of stomach cancer and made 40.9% in ulcerate infiltrative form, 54.5% – diffuse infiltrative tumor growth. Metastases in 10th group of lymph nodes observed in low-grade differentiated tumors up to 86.4% cases.
Conclusion: the performance of principle splenectomy in extensive gasterectomy has been induced in the following cases. Cancer of proximal part of stomach T3-T4, low differentiated structure, infiltrative growth, stomach cancer of total affection; infiltrative form of diffuse type structure stomach cancer, any localization.

6584 POSTER

A phase III study of CapeOx +/− lapatinib in HER2 positive locally-advanced/metastatic upper gastrointestinal adenocarcinoma: interim safety results

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Background: HER2 overexpression or amplification is associated with worse prognosis in locally advanced/metastatic adenocarcinoma of the upper gastrointestinal (UGI). Fluoropyrimidine plus platinum-based treatment is the backbone therapy for the treatment of this disease with a median survival rate of less than a year. LOGiC/TRIO-13 is a phase III global trial in HER2 positive UGI adenocarcinoma randomizing patients to capecitabine and oxaliplatin (CapeOx) with lapatinib or placebo (PBO) designed to evaluate safety and efficacy. A preplanned interim analysis of safety was conducted to evaluate tolerability of this novel regimen.
Methods: CapeOx was administered in a 3-week cycle. Oxaliplatin (130 mg/m^2) was administered on day 1; capecitabine (850 mg/m^2/BID) on day 1−14; and lapatinib (1250 mg) or PBO daily on day 1 onward. The safety analysis was performed after twenty randomized subjects completed 1 cycle of therapy.
Results: From September 2008 to February 2009, 22 subjects with metastatic gastric/GEJ/esophageal (n = 17/3/2, respectively) were randomized; median age 59 (range: 43−80; 17 males); ECOG PS 0 (n = 10), 1 (n = 11), 2 (n = 1);); 21 pts comprise the safety population (1 pt withdrew prior to study therapy); of these, 2 subjects reported significant toxicities defined as severe adverse events. The most common treatment emergent adverse events (TEAE) included neuropathy (gr1, n = 8), diarrhea (g1−2, n = 9; gr3, n = 2 pts); nausea (g1−2, n = 8; g3, n = 3); vomiting (g1−2, n = 9); anorexia (g1−2, n = 4; gr3, n = 2). Additional g3 events included asthenia (n = 1); dehydration (n = 1); pulmonary embolism (n = 1), renal failure (g3−4, n = 2); No unexpected toxicities occurred.
Conclusion: Twenty-one subjects received at least 1 cycle of treatment. Only 2 had significant toxicity, similar to expected based on studies with CapeOx alone. No unusual toxicities were observed. The regimen CapeOx plus lapatinib/PBO appears well-tolerated in patients with HER2-positive UGI cancers.

6585 POSTER

Changes in body composition following Whipple's procedure in patients with pancreatic cancer

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Background: Pancreatic cancer (PC) is a devastating disease with surgical resection providing the only possible cure. The Whipple's Procedure (WP) is one of the most common resection procedures performed in PC patients. Recovery following a WP may be determined by the patient's nutritional status. The restoration of protein and fat losses should improve the patient's response to adjuvant therapy, which is mandatory when margins are involved. It is, therefore, important to investigate the effect(s) of margin involvement on long-term nutritional status through detailed and comprehensive body composition analysis.
Aims: The primary aim of this project, therefore, was to investigate and describe the detailed body composition (BC) changes that occur during the first six months after a WP for PC as well as determining the differences in BC of patients with Clear Margins (CM) and Unclear Margins (UCM) during this period.
Methods: 27 (14 males, 13 females) consecutive PC patients undergoing WP were recruited. Surgery resulted in 10 patients with UCM and 17 with CM. BC measurements were performed at base-line and then at 2, 5, 14, and 26 weeks post-operative time-points. BC measurements included Fat Mass (FM), Nitrogen Index (NI), Lean Body Mass (LBM), Total Body Water (TBW), Total Body Potassium (TBK) weight and Body Mass Index (BMI). Changes in BC within as well as between the groups were measured and compared statistically.
Results: There were significant differences between the groups in BMI (p = 0.048l; p = 0.035), FM (p = 0.027; p = 0.044), and weight (p = 0.047; p = 0.041) at the base-line and two weeks post-operative time-points,