developed metachronous EC and local recurrence, respectively. Apart from one, they could be retreated endoscopicaly.
Conclusions: EMR is a very useful therapeutic modality for cSt I EC, not only for local control but also as a clinically sufficient treatment; especially in pts. with severe concurrent disease.

6575 POSTER

Bevacizumab combined with chemotherapy in the treatment of advanced/metastatic gastro-entero-pancreatic tumours: interim safety results from the phase II BETTER study

E. Mitry[1], M. Ducreux[2], S. Dominguez[3], C. Louvet[4], J.F. Seitz[5], D. Smith[6], J.E. Kurtz[7], C. Lombard-Bohas[8], P. Ruszniewski[9], D. O'Toole[10]. *[1]Ambroise-Paré University Hospital, Department of Gastro-Enterology and Digestive Oncology, Boulogne-Billancourt, France; [2]Gustave Roussy Cancer Clinic, Department of Gastro-Enterology, Villejuif, France; [3]Oscar Lambret Cancer Clinic, Department of Digestive and Urologic Oncology, Lille, France; [4]Saint-Antoine University Hospital, Department of Oncology, Paris, France; [5]La Timone University Hospital, Department of Digestive Oncology, Marseille, France; [6]Bordeaux University Hospital, Department of Medical Oncology and Radiotherapy, Bordeaux, France; [7]Strasbourg University Hospital, Department of Hematology and Oncology, Strasbourg, France; [8]Edouard Herriot University Clinic, Department of Hepato-Gastro-Enterology, Lyon, France; [9]Beaujon University Hospital, Department of Pancreato-Gastro-Enterology, Clichy, France; [10]St James's Hospital & Trinity College, Gastrointestinal Medical and Surgical Department, Dublin, Ireland*

Background: Gastro-entero-pancreatic (GEP) tumours are known to be highly vascular with elevated expression levels of vascular endothelial growth factor (VEGF). The aim of this study was to assess the efficacy and safety of adding bevacizumab (BV), a VEGF inhibitor, to two chemotherapy regimens in patients (pts) with previously untreated, progressive locally advanced/metastatic well-differentiated GEP tumours (pancreatico-duodenal and gastrointestinal [GI] tract).
Materials and Methods: Prospective, open-label, two-arm, non-comparative, multicentre phase II trial (EUDRACT 2007–003381−18). Pts with pancreatico-duodenal tumours received 5-FU 400 mg/m^2/day + streptozotocin 500 mg/m^2/day every 6 weeks + BV 7.5 mg/kg i.v. every 3 weeks (Arm 1); pts with GI tract tumours received capecitabine 1000 mg/m^2 per day on days 1−14 + BV 7.5 mg/kg i.v. every 3 weeks (Arm 2). After 6 months of treatment the physicians judged whether further chemotherapy was required. BV was administered until disease progression, unacceptable toxicity, or pt or physician decision to discontinue. The primary endpoint was progression-free survival. Secondary endpoints included response rate, overall survival and safety. The trial was funded by Roche France.
Results: Here we report interim safety findings on the first 40 pts enrolled (from a planned total of 81 pts) between June 07 and May 08. These findings relate to the first 6 months of treatment. Baseline characteristics are as follows: 21 male, 19 female; median age 59 years (range 37−82); 20 pancreatico-duodenal, 20 GI tract tumours. Grade 3/4 adverse events (AEs) were observed in 10 pts (50%) in Arm 1 and 12 pts (60%) in Arm 2. Main grade 3/4 AEs included hypertension (2 pts in Arm 1, 5 pts in Arm 2), asthenia (1 in Arm 1, 2 in Arm 2), embolism (1 in each Arm), haemorrhage (1 in each Arm), abdominal pain (1 in Arm 1), nausea (1 in Arm 1), diarrhea (2 in Arm 2) and febrile neutropenia (1 in Arm 2). Grade 3/4 BV-related AEs were observed in 3 pts in Arm 1 and 5 pts in Arm 2. Serious AEs were reported in 3 pts in each arm (1 BV-related SAE in Arm 1 and 2 in Arm 2). Treatment discontinuation due to toxicity was reported in 2 pts in Arm 1 and 1 pt in Arm 2. One pt died due to BV-related haemorrhagic stroke.
Conclusions: These results showed no unanticipated toxicity with BV plus standard chemotherapy for pts with previously untreated, progressive locally advanced/metastatic well-differentiated GEP tumours.

6576 POSTER

Irinotecan and low-dose capecitabine combination as first-line chemotherapy in advanced or metastatic gastric cancer: results of a phase II study

F. Farhat[1], J. Kattan[2], G. Chahine[2], F. Naser[2], F. Youness[3], M. Ghosn[2]. *[1]Hammoud Hospital UMC, Hemato-Oncology, Saida, Lebanon; [2]Hotel Dieu de FRANCE, Hemato-Oncology, Beirut, Lebanon; [3]Cancer Research Group – Collaborative Group, Hemato-Oncology, Beirut, Lebanon*

Background: Chemotherapy has a proven palliative role in advanced or metastatic gastric cancer. However, none of the currently explored regimens have shown compelling improvements without an impact on patients' quality of life. This phase II pilot study investigated the combination of irinotecan (CPT11) plus low-dose capecitabine as first-line therapy in advanced or metastatic gastric cancer.
Materials and Methods: For a period of 3 years patients with advanced or metastatic gastric cancer were enrolled to receive a combination of irinotecan 80 mg/m^2 on days 1, 8 and 15 plus capecitabine 625 mg/m^2 twice daily on days 1−14 every 4 weeks for a maximum of 8 cycles. Outcomes included response rate, time to progression, overall survival and safety. Outcomes were evaluated every 2 cycles.
Results: 32 patients, with a median age of 55 years, were evaluable. A total of 153 cycles were administered with a median of 4.7 cycles per patient. The objective response rate was 47%, with 9 patients having stable disease. The overall tumour control rate was 75%. Median time to progression and overall survival were 5 months and 8 months, respectively. Treatment was well tolerated with only 7 reported cases of grade 3/4 toxicities. No treatment-related deaths or hand-foot syndrome were observed during the study. Grade 3/4 toxicities were neutropenia (2 patients), diarrhoea (2 patients), nausea and vomiting (2 patients), asthenia (1 patient). Dose reduction was required for at least one cycle in 7 cases (22%).
Conclusion: The monthly regimen of low-dose capecitabine plus irinotecan appears to be active with a good toxicity profile in the treatment of advanced or metastatic gastric cancer. In cases where there is contraindication of platinum-based therapy, the more recent oxaliplatin- or docetaxel-based chemotherapies can be applied to this regimen.

6577 POSTER

A randomized phase II trial of weekly docetaxel plus either cisplatin or oxaliplatin in patients with previously untreated advanced gastric cancer: Preliminary results

S. Sym[1], S. Park[2], J. Park[1], Y. Park[1], I. Jung[1], E. Cho[1], W. Lee[3], M. Chung[3], D. Shin[3], J. Lee[3]. *[1]Gachon University Gil Hospital, Internal Medicine, Incheon, Korea; [2]Sungjyunkwan University Samsung Medical Center, Internal Medicine, Seoul, Korea; [3]Gachon University Gil Hospital, Surgery, Incheon, Korea*

Background: Docetaxel, in combination with cisplatin or oxaliplatin, has demonstrated efficacy against advanced gastric cancer (AGC). This randomized phase II trial evaluated two weekly docetaxel-based regimens to see which would be most promising according to objective response rate (ORR) as first-line therapy in AGC.
Methods: Chemotherapy-naïve patients with measurable unresectable and/or metastatic gastric adenocarcinoma and a performance status $\leqslant 2$ were randomly assigned to receive docetaxel (35 mg/m^2) weekly on days 1 and 8 of a 21-day cycle plus either cisplatin (60 mg/m^2 on day 1) (arm A) or oxaliplatin (120 mg/m^2 on day 1) (arm B). Toxicity was assessed on days 1, 8, and 21 of each cycle, and response was evaluated every 2 cycles.
Results: Between March 2007 and April 2009, 75 eligible patients entered. In Arm A, 35 patients were evaluable for objective response and 36 for safety. In Arm B, 37 patients were evaluable for objective response and 37 for safety. Median age was 57 years and disease status was comparable for both arms. Fourteen of 35 (40.0%) patients had a confirmed objective response in the arm A (95% confidence interval [CI] 23.7−56.2%) and 16 of 37 (43.2%) patients had a confirmed objective response in the arm B (95% CI 27.2−59.2%). No significant difference was noted between the arms both for ORR ($p = 0.641$) or for disease control (62.9% and 81.1%, respectively, $p = 0.116$). Median progression free survival time was 4.8 month in the arm A and 4.3 months in the arm B (Hazard ratio = 1.040; 95% CI, 0.602−1.797; $p = 0.889$). Median overall survival time was 9.6 months in the arm A and not reached in the arm B (Hazard ratio = 0.501; 95% CI, 0.243−1.036; $p = 0.062$). There was no relevant difference in the occurrence of overall grade 3/4 toxicity between the two arms (58.3% vs. 54.1%, respectively; $p = 0.815$). Neutropenia was the most common grade 3/4 toxicity (33.3% vs. 37.8%, respectively). There was one treatment related death in each arm.
Conclusions: The preliminary results showed that both treatment arms have similar clinical efficacy as front-line treatment in AGC. Each regimen has a manageable tolerability profile. The accrual is ongoing.

6578 POSTER

A randomized phase II study of irinotecan monotherapy versus irinotecan plus 5-fluorouracil/leucovorin combination as a salvage chemotherapy in previously treated patients with advanced/metastatic gastric cancer

Y. Park[1], S. Sym[1], J. Park[1], E. Cho[1], D. Shin[1], J. Lee[1]. *[1]Gachon Medical School Gil Medical Center, Internal Medicine, Incheon, Korea*

Background: The purpose of this study was to compare the efficacy and toxicity of adding 5-fluorouracil/leucovorin to irinotecan in locally advanced/metastatic gastric cancer as a salvage chemotherapy.
Materials and Methods: Eligible patents had performance status 0 to 2, measurable unresectable and/or metastatic gastric adenocarcinoma,

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

M. Möhler[1], A. Mueller[2], T. Trarbach[3], T. Seufferlein[4], S. Kubicka[5], F. Lordick[6], M. Geissler[7], S. Daum[8], P.R. Galle[2], S. Kanzler[2]. *[1]University Hospital Mainz, 1. Med. Klinik und Poliklinik, Mainz, Germany; [2]University Hospital Mainz, Medical Department, Mainz, Germany; [3]University Hospital Essen, Medical Department, Essen, Germany; [4]University Hospital Halle, Medical Department, Halle, Germany; [5]University Hospital Hannover, Medical Department, Hannover, Germany; [6]University Hospital Heidelberg, Medical Department, Heidelberg, Germany; [7]City Hospital Esslingen, Medical Department, Esslingen, Germany; [8]University Hospital Berlin, Medical Department, Berlin, Germany*

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

K. Amagai[1], R. Matsumoto[1], M. Oozeki[1], S. Fujieda[1], M. Araki[1], M. Goto[1]. *[1]Ibaraki Prefectural Central Hospital and Cancer Center, Gastroenterology and GI Oncology, Kasama, Japan*

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

R. Pazo-Cid[1], A. Godoy[2], J. Lao Romera[1], N. Fernandez-Mosteirin[2], T. Puértolas[1], V. Calderero[1], R. García-Foncillas[3], J.f. Lucia[2], M.j. Lecumberri[1], A. Antón[1]. *[1]Hospital Universitario Miguel Servet, Medical Oncology, Zaragoza, Spain; [2]Hospital Universitario Miguel Servet, Hematology, Zaragoza, Spain; [3]Zaragoza University, Biostatistics, Zaragoza, Spain*

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).