

and adequate organ function. Irinotecan (150 mg/m²) was given on first day, repeated every 2 weeks in irinotecan monotherapy group (arm A), and irinotecan (150 mg/m²) was given on first day with leucovorin (folinic acid) (20 mg/m²) followed by 5-FU (2000 mg/m² 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, 17 patients 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 0–37%). 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. Möhler¹, A. Mueller², T. Trarbach³, T. Seufferlein⁴, S. Kubicka⁵, F. Lordick⁶, M. Geissler⁷, S. Daum⁸, P.R. Galle², S. Kanzler². ¹University Hospital Mainz, 1. Med. Klinik und Poliklinik, Mainz, Germany; ²University Hospital Mainz, Medical Department, Mainz, Germany; ³University Hospital Essen, Medical Department, Essen, Germany; ⁴University Hospital Halle, Medical Department, Halle, Germany; ⁵University Hospital Hannover, Medical Department, Hannover, Germany; ⁶University Hospital Heidelberg, Medical Department, Heidelberg, Germany; ⁷City Hospital Esslingen, Medical Department, Esslingen, Germany; ⁸University 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/m²) combined with chemotherapy of irinotecan (80 mg/m²) + 24 hour continuous infusion of sodium folinic acid (Na-FA: 200 mg/m²) and 5-FU (1500 mg/m²) 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 had 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. Amagai¹, R. Matsumoto¹, M. Oozeki¹, S. Fujieda¹, M. Araki¹, M. Goto¹. ¹Ibaraki 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/m² daily was administered orally in two divided doses for 2 weeks, followed by a 2-weeks rest. Cisplatin at 30 mg/m² 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-Cid¹, A. Godoy², J. Lao Romera¹, N. Fernandez-Mosteirin², T. Puértolas¹, V. Calderero¹, R. García-Foncillas³, J.f. Lucia², M.j. Lecumberri¹, A. Antón¹. ¹Hospital Universitario Miguel Servet, Medical Oncology, Zaragoza, Spain; ²Hospital Universitario Miguel Servet, Hematology, Zaragoza, Spain; ³Zaragoza 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-fluoropyrimidine-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 ($p<0.05$).