3541 POSTER

HER2-positive advanced gastric cancer: similar HER2-positivity levels to breast cancer

F. Lordick[1], Y.J. Bang[2], Y.K. Kang[3], D. Otero Reyes[4], G.M. Manikhas[5], L. Shen[6], E. Kulikov[7], O. Stoss[8], B.W.M. Jordan[9], E. Van Cutsem[10]. *[1]Munich University of Technology, Oncology, Munich, Germany; [2]Seoul National University Hospital, Oncology, Seoul, South Korea; [3]Asan Medical Centre, Oncology, Seoul, South Korea; [4]Hospital CIMA, Oncology, San José, Costa Rica; [5]St Petersburg City Oncology Hospital, Department of Oncogynaecology, St Petersburg, Russian Federation; [6]Peking University School of Oncology, Department of Gastrointestinal Oncology, Beijing, China; [7]Ryazan State IP Pavlov Medical University, Oncology, Ryazan, Russian Federation; [8]TARGOS Molecular Pathology GmbH, Oncology, Kassel, Germany; [9]F Hoffmann-La Roche, Oncology, Basel, Switzerland; [10]University Hospital Gasthuisberg, Oncology, Leuven, Belgium*

Background: To date, there has been no consensus on the rate of HER2 positivity in gastric cancer (GC). Previous studies have reported HER2 positivity in 6−35% of GC tumours, although sample sets have been small and different methods of evaluation and scoring have been used. Accurate HER2 testing is important to identify patients eligible for treatment with trastuzumab (Herceptin®). The Phase III ToGA trial was designed to evaluate the combination of trastuzumab with standard fluoropyrimidine plus cisplatin chemotherapy for the treatment of advanced HER2-positive GC. Before initiating this trial, a validated methodology was set up for HER2 testing in advanced GC.
Methods: Following the validation study, standardised HER2 IHC (HercepTest™) and FISH (PharmDx™) protocols and scoring systems were established for GC (Hofmann et al. ASCO Gastrointestinal Cancers Symposium 2006. Abs 24). Tumour samples were collected from patients with GC, and centrally tested using both IHC and FISH to identify patients eligible for enrolment in the ToGA trial.
Results: To date, 1527 tumour samples have been assessed (341 HER2 positive; 1186 HER2 negative), giving an overall HER2-positivity rate of 22.3%. Both IHC and FISH results are available for 1425 patients, with 87% concordance. Differences were largely due to FISH-positive cases that were IHC 0/1+. HER2 positivity differed significantly by histological subtype: 34% in intestinal, 6% in diffuse and 20% in mixed. HER2 positivity also varied according to the site of the tumour: 32% (23/72) in gastro-oesophageal junction tumours and 18% (149/817) in gastric tumours. The HER2-positivity rate was similar in specimens obtained by biopsy (242/1027; 24%) and surgery (95/477; 20%).
Conclusions: Using validated protocols and based on the large sample set from the ongoing ToGA trial, the observed overall HER2-positivity rate in advanced GC is as high as in breast cancer at ~22%. First efficacy data from the ToGA trial are expected in 2009.

3542 POSTER

Preliminary results from a phase II study of sunitinib as second-line treatment for advanced gastric cancer

Y. Bang[1], Y. Kang[2], W. Kang[3], N. Boku[4], H. Chung[5], J. Tursi[6], M.J. Lechuga[6], L. Verkh[7], R. Chao[8], A. Sobrero[9]. *[1]Seoul National University, Hospital, Seoul, South Korea; [2]Asan Medical Center, Medical, Seoul, South Korea; [3]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [4]Shizuoka Cancer Center, 1007 Shimonagakubo, Shizuoka, Japan; [5]Cancer Metastasis Research Center, Yonsei Cancer Center, Seoul, South Korea; [6]Pfizer Italy, Clinical Research Oncology, Milan, Italy; [7]Pfizer Inc, Pfizer Clinical Pharmacology, La Jolla, USA; [8]Pfizer Inc, Pfizer Global Research & Development, La Jolla, USA; [9]Department of Medical Oncology, Ospedale San Martino, Genoa, Italy*

Background: Sunitinib malate (SUTENT®; SU), an oral, multitargeted tyrosine kinase inhibitor of VEGFRs, PDGFRs, KIT, RET and FLT3, is approved for the treatment of advanced RCC and imatinib-resistant or -intolerant GIST. Preliminary results from a phase II, open-label, multicenter study investigating the safety and activity of SU monotherapy in patients (pts) with previously treated gastric cancer are reported here.
Patients and Methods: Pts with measurable stage IV disease, 1 prior chemotherapy regimen and ECOG PS < 1 were enrolled. SU 50 mg/day for 4 weeks followed by 2 weeks off treatment was administered in 6-week cycles (4/2 schedule). A Simon 2-stage design (target accrual 38 pts in the first stage) was used and the cohort was expanded to 63 pts if $\geqslant$2 partial responses (PRs) were observed. The primary endpoint is RECIST-defined objective response rate. Secondary endpoints include duration of response, time-to-event rates and safety.
Results: As of April 2007, 42 pts (median age 56 years [range 25–78]; $\geqslant$2 metastatic sites, 74%; prior treatment with 5-FU $\pm$ platinum [P], 40%, capecitabine $\pm$ P, 17%, TS-1 $\pm$ P, 36%, other, 21%) are evaluable and have received a median of 2 SU cycles (range 1–6). PR was confirmed in 2 pts and 15 pts had stable disease (SD; 12 with SD for >3 months and 3 for >6 months) among 33 pts evaluable for efficacy. Median progression-free survival and overall survival were 12.3 weeks (range 10.1–18.4) and 50.7 weeks (range 28.0–not reached), respectively. Enrollment of the second cohort is ongoing. Common adverse events (AEs) were typically grade 1/2 in severity and included stomatitis, skin discoloration, fatigue, anorexia, diarrhea, hand–foot syndrome (HFS), nausea and vomiting. Grade 3/4 toxicities included HFS (9.5%), fatigue (9.5%), anorexia (9.5%) and mucosal inflammation (4.8%). Grade 3/4 hematological toxicities were neutropenia (31.0%), thrombocytopenia (26.2%) and anemia (14.3%). Of 7 pts experiencing serious SU-related AEs, 3 required dose modifications and 1 required treatment discontinuation. Preliminary PK investigations indicate that plasma drug concentrations seen in gastric cancer pts are similar to those in SU-treated pts with other tumor types.
Conclusions: Initial findings indicate that SU is generally well tolerated and shows promising signs of single-agent antitumor activity in gastric cancer pts following failure of chemotherapy. Further studies of SU in combination with standard chemotherapy are planned.

3543 POSTER

Phase I trial of capecitabine and gemcitabine with concurrent radical radiotherapy in locally advanced pancreatic cancer: final results

M. Michael[1], T. Price[2], T. Leong[3], V. Ganju[4], A. Strickland[5], M. Jefford[1], S. Ngan[3], A. Milner[6], J. Zalcberg[1]. *[1]Peter MacCallum Cancer Centre, Medical Oncology, Melbourne, Australia; [2]Queen Elizabeth Medical Centre, Medical Oncology, Adelaide, Australia; [3]Peter MacCallum Cancer Centre, Radiation Oncology, Melbourne, Australia; [4]Frankston Hospital, Medical Oncology, Melbourne, Australia; [5]Monash Medical Centre, Medical Oncology, Melbourne, Australia; [6]Peter MacCallum Cancer Centre, Biostatistics, Melbourne, Australia*

Background: Primary chemoradiation with infusional 5FU is widely used for the treatment of patients (pts) with locally advanced, unresectable pancreatic cancer (PaC), but with disappointing results. To improve efficacy and pt convenience novel chemotherapy regimens need to be evaluated in combination with radical radiotherapy (RT). The combination of capecitabine (Cap) (Xeloda®) and gemcitabine (G) has shown activity in advanced PaC and both agents are potent radiosensitisers. The aim of this phase I trial was to determine the MTD of the Cap plus G combination with concurrent RT in pts with localised PaC.
Patients and Methods: Eligible pts had unresectable, locally advanced PaC based on imaging and surgical staging, adequate organ function, ECOG PS 0−1 and no prior therapy. In combination with RT, G was escalated from 20 to 50 mg/m^2/day IV (days 1 and 4 of each week of RT), and Cap was escalated from 800 to 2000 mg/m^2/day (in 2 divided doses, days 1−5 of each week of RT) in 7 planned dose levels. RT consisted of 50.4 Gy/28 fractions/5.5 weeks using conformal techniques. Three pts were entered to each dose level. If 1 of 3 pts had a dose limiting toxicity (DLT) the cohort was expanded to 6 pts. DLTs were defined prospectively and based on treatment related toxicities and treatment interruptions.
Results: 18 pts have been accrued, with complete data on 15. Dose level 1: Cap/G; 800 mg/m^2/day/20 mg/m^2/day (3 pts). Dose level 2: 1,000/20 (10 pts). Dose level 3: 1,300/30 (5 pts). 3 pts (20%) had a PR, 8 pts (53%) had SD and 4 pts (27%) had PD. No DLTs were observed on dose levels 1 and 2, whilst 2 DLTs were observed in dose level 3; grade 3 dehydration (1 pt) and grade 3 diarrhoea (1 pt). Dose level 2 was declared the recommended dose level and was expanded to a total of 10 pts. No grade 3 or 4 haematological toxicities have been observed.
Conclusions: The addition of Cap and G to radical RT was both feasible and generally well tolerated. For future trials, Cap 1000 mg/m^2/day and G 20 mg/m^2/day (twice per week) is the recommended dose when combined with 50.4 Gy of RT. Final results and survival parameters will be presented.

3544 POSTER

Phase I study of gemcitabine as a fixed dose rate infusion and S-1 combination therapy in gemcitabine-refractory pancreatic cancer patients.

C. Morizane[1], T. Okusaka[1], J. Furuse[2], H. Ishii[2], H. Ueno[1], M. Ikeda[1], T. Ogura[1], K. Nakachi[2], E. Suzuki[2]. *[1]National Cancer Center Hospital, Hepatobiliary and Pancreatic Oncology Division, Tokyo, Japan; [2]National Cancer Center Hospital East, Hepatobiliary and Pancreatic Oncology Division, Kashiwa, Japan*

Background: Gemcitabine (Gem) monotherapy or Gem-containing chemotherapy is the standard first-line therapy for advanced pancreatic cancer