the triplet therapies containing capecitabine as compared with fluorouracil and for those containing oxaliplatin as compared with cisplatin.
Results: The hazard ratio for death in the capecitabine group was 0.88 (95% confidence interval [CI], 0.81 to 0.98) in comparison to fluorouracil and the hazard ratio for the oxaliplatin group was 0.93 (95% CI, 0.82 to 1.10) in comparison to cisplatin. Median survival times in the ECF, ECX, EOF, and EOX groups were 9.2 months, 9.3 months, 9.1 months, and 11.5 months, respectively; survival rates at 1 year were 36.6%, 38.9%, 40.1%, and 47.5%, respectively. Overall survival was longer with EOX than with ECF. Toxic effects of capecitabine and fluorouracil were almost similar. As compared with cisplatin, oxaliplatin was associated with lower incidences of grade 3 or 4 neutropenia, alopecia, renal toxicity but with slightly higher incidences of neuropathy.
Conclusions: In our experience, oxaliplatin and capecitabine are more effective than cisplatin and fluorouracil, respectively, in patients with previously untreated esophagogastric cancer.

6585 POSTER

Phase II Study of Low-dose Everolimus Plus Weekly Cisplatin and 24-hour Infusion of High-dose 5-fluorouracil and Leucovorin for First-line Treatment of Metastatic or Recurrent Gastric Cancers

K. Yeh[1], Y.C. Shen[1], C.P. Li[2], C.J. Yen[3], Y.L. Lin[1], Z.Z. Lin[1], L.T. Chen[4], W.C. Su[3], Y. Chao[5], A.L. Cheng[1]. *[1]National Taiwan University Hospital, Oncology, Taipei, Taiwan; [2]Taipei Veterans General Hospital, Gastroenterology, Taipei, Taiwan; [3]National Cheng Kung University Hospital, Oncology, Tainan, Taiwan; [4]National Health Research Institutes, Oncology, Tainan, Taiwan; [5]Taipei Veterans General Hospital, Cancer Center, Taipei, Taiwan*

Background: Cisplatin-HDFL regimen, using weekly 24-hour infusions of cisplatin and high-dose 5-fluorouracil (5-FU) and leucovorin, is commonly used in Taiwan for patients with advanced gastric cancer (GC), showing a satisfactory response rate with favourable toxicity profiles [J Clin Oncol 1994; 12(4): 875; J Clin Oncol (Suppl) 2006; 24(18S): A14063]. Everolimus (RAD001), a derivative of rapamycin, is an orally bioavailable mTOR inhibitor. We have demonstrated that low-dose everolimus (in concentration of 0.5 to 5.0 nM) has a chemosensitizing effect for cisplatin and 5-FU in GC cells [Proc Am Assoc Cancer Res 2007; 48: A4043].
Methods: All patients had pathologically confirmed metastatic/recurrent chemonaive GC, at least 1 measurable lesion, a fasting serum triglyceride level >70 mg/dl, ECOG PS 0/1/2, adequate hepatic, renal, and bone marrow functions. Everolimus 10 mg PO on days 1, 8, and 15; and was given concurrently with the initiation of chemotherapy. Cisplatin 35 mg/m^2 was given as a 24h infusion, days 1 and 8. A 24h infusion of 5-FU 2,000 mg/m^2 and leucovorin 300 mg/m^2 (HDFL) was given on days 1, 8, and 15. Cycles were repeated every 28 days, and response evaluation was performed every 2 cycles & at the end of protocol treatment. The primary end-point was confirmed objective response rate (RR) by RECIST.
Results: Between Mar. 2008 and Mar. 2011, 30 patients (M:15, F:15) with a median age of 55 (33−71) were enrolled and evaluable for response assessment. The overall RR was 60.0% (41−77%, 95% C.I.) with one CR and 17 PRs. Among a total of 201 cycles (median: 6, range: 1 to 25 cycles) given, Gr3/4 neutropenia, infection, nausea, and vomiting developed in 4.0%, 2.0%, 2.5%, and 2.5% of 201 cycles, respectively (data cut-off date: Mar. 31, 2011). None of them developed Gr3/4 stomatitis, diarrhea, or skin rash. Gastrointestinal and skin toxicities were generally mild with addition of low-dose weekly everolimus to cisplatin-HDFL. Gr1/2 nausea, vomiting, stomatitis, and diarrhea developed in 18.9%, 15.4%, 12.9%, and 6.0% of 201 cycles, respectively. Gr1/2 skin rash and Gr1 hand-foot syndrome developed in 7.0% and 30.8% of 201 cycles, respectively. One patient has developed reversible HDFL-related hyperammonemic encephalopathy. Median PFS (range: 1.2 to 24.3+ months) and OS (range: 1.8 to 24.3+ months) was 7.2 and 12.6 months, respectively.
Conclusions: Low-dose everolimus plus infusional cisplatin-HDFL is a highly effective regimen with low toxicity and favorable survival in first-line treatment of metastatic or recurrent GC. Addition of low-dose weekly everolimus to infusional cisplatin and HDFL did not cause any additional gastrointestinal toxicity.

6586 POSTER

Metronomic Combination Chemotherapy With S-1 and Biweekly Paclitaxel for Advanced Gastric Cancer

N. Takiguchi[1], M. Nagata[1], Y. Nabeya[1], O. Kainuma[1], A. Ikeda[1], H. Soda[1], A. Cho[1], T. Iwase[1], H. Yamamoto[1], T. Denda[2]. *[1]Chiba Cancer Center, Gastroenterological Surgery, Chiba, Japan; [2]Chiba Cancer Center, Gastroenterological Internal Medicine, Chiba, Japan*

Background: The recent phase III chemotherapy trials for gastric cancer have showed the median survival time is prolonged up to 13 months by SPIRITS trial (addition of cisplatin to S-1)and the START trial (addition of docetaxel to S-1).
However, the gastric cancer patients cannot often keep enough oral intakes by primary disease itself. The adverse drug reactions of chemotherapy more strongly develop, and the continuation of the chemotherapy becomes often difficult.
To get the better prognosis, we think the chemotherapy with few side effects and high treatment feasibility is demanded. The metronomic combination chemotherapy with S1 and Paxlitaxel (PTX) has been treated for advanced gastric cancer at our hospital. We aimed to evaluate the efficacy of this treatment.
Materials and Methods: Fifty two advanced gastric cancer patients were examined. S-1 at 80 mg/m^2 daily was given orally, twice daily for consecutive 7 days, and PTX at 80 mg/m^2 was administered by intravenous drip infusion on day 1, followed by a 1-week rest period. This treatment was repeated every 2 weeks (one cycle each) until disease progression or unacceptable toxicity was seen.
Results: A total of 1146 cycles were administered, with a median of 22 cycles (range: 5−76) per patient. Three patients had complete responses and 23 patients had partial responses. Six patients kept in stable desese. The response rate was 61.5% (32/52) and the median time to treatment failure was 9.8 months. The median over all survival time was 21.9 months. The one-year survival rate was 78.8%. The median survival times according to Performance Status (PS) were 25.5 months in PS0, 19.3 months in PS1, and 9.3 months in PS2, respectively. The major adverse reactions were leucopenia and neutropenia. Adverse reactions as gastrointestinal symptoms were few.
Conclusion: The metronomic combination of S-1 and biweekly PTX therapy for advanced gastric cancer appears to be highly efficacious and safe with high treatment continuity and QOL.

6587 POSTER

A Phase 1b, Open-Label Study to Evaluate the Safety of Ganitumab (AMG 479) in Combination With Gemcitabine as First-line Therapy in Patients With Metastatic Pancreatic Cancer

M. Ikeda[1], T. Okusaka[2], A. Fukutomi[3], S. Otani[4], K. Shibayama[4], T. Takubo[5], J. Gansert[6]. *[1]National Cancer Center Hospital East, Hepatobilinary and Pancreatic Medical Oncology Division, Kashiwa, Japan; [2]National Cancer Center Hospital, Department of Hepatobiliary and Pancreatic Oncology, Tokyo, Japan; [3]Shizuoka Cancer Center, Department of Gastrointestinal Oncology, Nagaizumi, Japan; [4]Takeda Bio Development Center Limited, Clinical Development Division, Tokyo, Japan; [5]Takeda Bio Development Center Limited, Medical Sciences Division, Tokyo, Japan; [6]Amgen Inc., Oncology Therapeutics, Thousand Oaks CA, USA*

Background: Ganitumab (AMG 479) is a fully human monoclonal antibody against human IGF-1R that inhibits the survival and proliferative signals driven by IGF-1 and -2. This is the first study to assess the safety and tolerability of ganitumab 20 mg/kg in combination with gemcitabine in Japanese patients (pts) with metastatic pancreatic cancer (mPC).
Material and Methods: Six previously untreated mPC pts were to receive gemcitabine at 1,000 mg/m^2 on days 1, 8 and 15 followed by ganitumab at 20 mg/kg on days 1 and 15, every 28 days cycle. Dose-limiting toxicity (DLT) was assessed in cycle 1.
Results: Six pts [5 male; median age 62 (range, 43 to 69), ECOG PS 0−1] were enrolled, and received >1 dose of ganitumab combined with gemcitabine. The median number of doses administered of ganitumab was 4.5 (range: 3 to 7) and gemcitabine was 6 (range: 4 to 10). The median relative dose intensity of ganitumab was 1.0 (range, 0.6 to 1.0) and gemcitabine was 0.93 (range, 0.7 to 1.0). One pt had a DLT of grade 3 neutropenia with fever >38.5ºC. One pt experienced treatment related serious adverse event of grade 3 nausea and grade 3 decreased appetite in post DLT evaluation period. All 6 pts experienced treatment-emergent adverse events (AEs); the grade $\geqslant$ 3 AEs were neutropenia (4 pts), thrombocytopenia (2), leucopenia (1), lymphopenia (1), nausea (1), blood sodium decreased (1), and decreased appetite (1). Four pts experienced infusion reactions. No developing anti-ganitumab antibodies were detected. Preliminary pharmacokinetic (PK) analysis for ganitumab indicated mean C_{max} and AUC_{0-336} were 309 μg/mL and 1299 day·μg/mL, respectively. Effect of ganitumab on gemcitabine PK was not clearly observed.
Conclusions: Ganitumab 20 mg/kg in combination with gemcitabine 1,000 mg/m^2 (which is one regimen in the phase 3 GAMMA (gemcitabine and AMG 479 in metastatic adenocarcinoma of the pancreas) study) was tolerable for pts with mPC. Updated information will be presented at the meeting.