gastrointestinal tumors

FIVE-YEAR RESULTS OF THE RANDOMIZED PHASE III TRIAL COMPARING S-1 MONOTHERAPY VERSUS SURGERY ALONE FOR STAGE II/III GASTRIC CANCER PATIENTS AFTER CURATIVE D2 GASTRECTOMY (ACTS-GC STUDY)

M. Sasaki1, T. Kinoshiba2, H. Furukawa3, T. Yamaguchi4, A. Nashimoto5, M. Fujiwara1, T. Nakajima6, Y. Chashu7
1Surgery, Hyogo College of Medicine, Nishinomiya/JAPAN, 2Upper Abdominal Surgery, National Cancer Center Hospital East, Kawasaki/JAPAN, 3Surgery, Sakai Municipal Hospital, Sakai/JAPAN, 4Surgery, Cancer Institute Hospital, Tokyo/JAPAN, 5Nagata Cancer Center Hospital, Nagata/JAPAN, 6Surgery, Nihon University School of Medicine, Tokyo/JAPAN, 7Cancer Institute Hospital, Surgery, National Cancer Center Hospital East, Kashiwa/JAPAN, 3Surgery, University of Tokyo, Tokyo/JAPAN, 2Upper Abdominal Surgery, Ospedali Riuniti, Bergamo/ITALY, 4U.O. Oncologia Medica, Uni. Politecnica delle Marche, Ancona/ITALY, 5Department of Medical Oncology, Ospedale S. Martino, Genova/ITALY, 6Medical Oncology Department, Azienda Ospedaliera Treviso-Caravaggio, Treviso/ITALY, 7Ospedale C. Poma, Mantova/ITALY, 8Graduate School of Medicine and Faculty of Medicine, the University of Tokyo, Tokyo/JAPAN, 9Istituto Mario Negri, Milano/ITALY, 10Universita` Politecnica delle Marche, Ancona/ITALY

Background: The results of the first interim analysis of the ACTS-GC study was reported in ASCO-GI meeting in 2007 and published soon after (Sakuramoto S et al. N Engl J Med 2007; 357:1810-20), as they showed significant survival benefit of S-1 monotherapy for stage II/III gastric cancer patients after D2 surgery. As 5 years have passed after completion of the enrollment, originally planned analysis was carried out using up-dated survival data to confirm the results and conclusion drawn from the interim analysis.

Method: Eligibility included R0 resection, pathological stage II/III (Japanese Classification, version 2), age ranged 20-80, no prior adjuvant treatment, adequate organ function. Pts were randomized to S-1 (80-120mg/day according to the body surface, 4 weeks administration with 2 weeks off in each course, starting within 45 days of surgery till 1 year after surgery,) or surgery alone (C). Primary end point was overall survival (OS). Assuming 500 pts in each, the study had 80% power to detect 0.70 HR for death to S-1 to C in OS at 5 year two-sided alpha.

Results: Between 10/2001 and 12/2004, 1059 pts were randomized (529 to S-1 and 530 to C). 25 pts were ineligible. There was no background difference between the groups. 474, 489, 175 pts were stage II, IIIA, IIIB respectively. 943(89%) pts could be followed up more than 5 years after surgery. Median follow-up time was 5.46 years. 139 and 196 pts died in S-1 and C group respectively. HR for death in S-1 to C in OS at 5 years was 0.65 (95%CI, 0.53-0.81).

At a median follow up of 13.4 months, 39 patients progressed in arm A and 40 in arm B. Median PFS was 4.5 months and 3.3 months respectively (HR=1.013; 0.68-1.55 CI 95%). Objective RR was 6.9% in arm A and 7.1% in arm B. Rate of responders/stable disease was 58.6% in arm A and 55.6% in arm B (P=0.47). Haematological and hepatic toxicity was the cause of discontinuation in 6 (10.3%) patients in arm A and 3 (8.9%) in arm B.

Conclusion: Addition of sorafenib to CT does not seem to significantly improve PFS and RR in advanced PC. The analysis of the molecular alterations of the RAS/RAF pathway is ongoing.

Disclosure: All authors have declared no conflicts of interest.

SORAFENIB DOES NOT IMPROVE THE RESULTS OF CHEMOTHERAPY IN ADVANCED PANCREATIC CANCER: A GISCAD RANDOMISED PHASE II TRIAL

R. Bernardi1, A. Sobrero2, R. Laibianca3, P. Bidoli4, S. Siena5, D. Ferrari6, S. Barni7, R. Cingolani8, M. Monterforte9, S. Cassiani10
1Clinica di Oncologia Medica, Universita` Politecnica delle Marche, Ancona/ITALY, 2Department of Medical Oncology, Ospedale S. Martino, Genova/ITALY, 3Medical Oncology, Ospedale Rovello, Bergamo/ITALY, 4U.O. Oncologia Medica, Monza/ITALY, 5Medical Oncology, Ospedale Negrada Ca` Grandis, Milan/ITALY, 6Ospedale San Paolo, Milano/ITALY, 7Medical Oncology Department, Azienda Ospedaliera Treviso-Caravaggio, Treviso/ITALY, 8Ospedale C. Poma, Mantova/ITALY, 9Istituto Mario Negri, Milano/ITALY, 10Università Politecnica Delle Marche, Clinica di Oncologia Medica, Ancona/ITALY

Background: No standard treatment is available for advanced pancreatic cancer (PC). Although gemcitabine (GEM) is used with the purpose of symptom palliation, there is no clear evidence of a significant survival increase. Attempts at improving results by combining GEM with other cytotoxic drugs failed to obtain any advantage. KRAS and BRAF mutations are present in approximately 90% and 5% of the PC respectively. Sorafenib is an inhibitor of the RAS/RAF signalling pathway showing inhibition of proliferation of pancreatic tumour cell lines containing KRAS or BRAF mutations. It may be combined with gemcitabine and cisplatin without any pharmacokinetic interaction or enhanced toxicity. Therefore, a phase II randomised trial was designed to explore the role of sorafenib in combination with chemotherapy (CT).

Methods: Patients with histologically proven, locally advanced or metastatic PC, chemonaive and ECOG 0-2 were eligible. Subjects were randomized to receive gemcitabine 25 mg/m2/day and GEM 1000 mg/m2/day on d1-4q21days plus Sorafenib at 400 mg (2 tabletsx200 mg each) orally twice daily continuously (arm A) or GEM/cisplatin alone (arm B). The primary end point was Progression Free Survival (PFS), other end points were response rate (RR) and overall survival.

Results: 114 patients were enrolled. Patients characteristics are summarized in the table.

At a median follow up of 3.4 months, 39 patients progressed in arm A and 40 in arm B. Median PFS was 4.5 months and 3.3 months respectively (HR=1.013; 0.68-1.55 CI 95%). Objective RR was 6.9% in arm A and 7.1% in arm B. Rate of responders/stable disease was 58.6% in arm A and 55.6% in arm B (P=0.47). Haematological and hepatic toxicity was the cause of discontinuation in 6 (10.3%) patients in arm A and 3 (8.9%) in arm B.

Conclusion: Addition of sorafenib to CT does not seem to significantly improve PFS and RR in advanced PC. The analysis of the molecular alterations of the RAS/RAF pathway is ongoing.

Disclosure: All authors have declared no conflicts of interest.
Background: WX-671 (Mesupron) is an orally available prodrug of WX-UKI, a serine protease inhibitor that inhibits uPA as well as other serine proteases. WX-UKI (Stryker-Han et al., Thromb Haemost 2005) and WX-671 have shown to efficiently reduce primary tumor growth and metastasis formation in a variety of animal models. The proteolytic factor uPA and its inhibitor PAI-1 belong to those biological factors which have provided the highest level of evidence (LOE1) in terms of their prognostic and predictive significance. WX-671 is currently the only drug in Phase II aiming at this target.

Methods: 95 patients with locally advanced non-metastatic pancreatic cancer were randomized to three cohorts receiving daily oral WX-671 as hydrogen sulphate corresponding to 200 and 400 mg WX-671 free base or no WX-671. In addition, all patients were treated with weekly gemcitabine (1000 mg/m² i.v. as per SPC). Treatment continued until disease progression or toxicity. Safety was assessed by measuring vital signs, laboratory parameters (hematology, blood chemistry, coagulation) and ECOG. Efficacy endpoints were response rate at the various staging intervals, progression free survival, time to first metastasis, overall survival as well as changes in tumor- and uPA-system-related markers.

Results: All 95 patients were accrued between Jun 2007 and Aug 2008. Efficacy was assessed by a central reader at regular intervals based on digital CT images. Data collection has been closed in Jan 2010. Response rate of the combination was 12.9 % compared to 3.8% for Gemcitabine alone. 1-year PFS rate was increased from 16.2% (Gemcitabine) to 26.9% for the combination of gemcitabine with 400 mg WX-671. Overall survival showed an increase of 9.9 mg (gemcitabine alone) to 12.5 mg for the combination of gemcitabine and WX-671. 1-year survival increased from 33.9% with gemcitabine to 50.6% for the combination.

Conclusions: The combination of daily oral WX-671 in combination with weekly i.v. gemcitabine was well tolerated and demonstrated anti-tumor activity which led to promising increase in overall survival.

Disclosures: C. Male: Wiley AG, Director Clinical Research; N. Neville: Wiley AG, Vice President CR; P. Bevan: Wiley AG, Director. All other authors have declared no conflicts of interest.

Conclusion: In the entire study population, OS was not improved with the addition of bev, although there were significant improvements in PFS and ORR. Regional differences in efficacy are noted, and further subgroup analysis is ongoing, including biomarker analysis, in order to understand the potential role of bev in AGC.

Disclosures: E. van Cutsem: Member on Advisory board: Roche Corporate-sponsored research with Roche; M. Shah: Corporate-sponsored research with Genentech; V. Kang: Member on Advisory board: Roche Honoria from Roche; J. Wu: Employed by Roche; B. Langer: Employed by Roche. All other authors have declared no conflicts of interest.

Combination chemotherapy is widely accepted for patients with advanced gastric cancer, but uncertainty remains regarding the choice of the regimen.

Objectives: To assess the effect of: Comparison 1) irinotecan versus non-irinotecan-containing regimens, comparison 2) docetaxel versus non-docetaxel-containing regimens, comparison 3) regimens containing oral 5-FU prodrugs versus intravenous fluoropyrimidines, comparison 4) oxaliplatin versus cisplatin-containing regimens on overall survival.

Keywords: Gastrointestinal malignancies, Drug therapy, Systemic treatment, Advanced gastric cancer

Background: Median survival for pts with inoperable AGC in most phase III studies is <1 year. The addition of bev to chemotherapy (chemo) is supported by a strong preclinical rationale and phase II evaluation. AVAGAST compared the efficacy/safety of chemo vs pl and chemo vs bev (table). While the primary endpoint was not met, median OS and PFS were different across regions (table). Safety analyses did not reveal any new findings and an acceptable safety profile was found for chemo + bev (table).
EPIRUBICIN (E) IN COMBINATION WITH CISPLATIN (CDDP) AND CAPECITABINE (C) VERSUS DOCETAXEL (D) COMBINED WITH 5-FLUOROURACIL (5-FU) BY CONTINUOUS INFUSION (C.I.) AS FRONT-LINE THERAPY IN PATIENTS WITH ADVANCED GASTRIC CANCER (AGC): PRELIMINARY RESULTS OF A RANDOMISED PHASE II TRIAL OF THE GRUPPO ONCOLOGICO DELL’ITALIA MERIDIONALE

N. Silvestris1, F. De Vita2, M.P. Romano3, E. Maecillo3, V. Gembia4, V. Lorusso4, S. Greco4, F. Gisineri4, M. Ordinari4, G. Colucci4

1Medical and Experimental Oncology Unit, Cancer Institute “Giovanni Paolo II”, Bari/ITALY, 2Medical Oncology Unit, University of Naples, Naples/ITALY, 3Hospital Casa Sollievo della Sofferenza, San Giovanni Rotondo/ITALY, 4Casa di cura la Madalena, Paleova/ITALY, 5Medical Oncology, Ospedale Vai, Lecce/ITALY, 6U.O.C. Oncologia, Ospedali, Bindisi/ITALY, 7Medical and Experimental Oncology Unit, Cancer Institute, Bari/ITALY, 8Intemistica Clinica E Sperimentale, Second University of Naples, Naples/ITALY, 9Medical Oncology, Oncology Institute, Bari/ITALY

Background: Results of randomised phase III trials support the use of systemic chemotherapy as palliative treatment of patients with AGC with remission rates of 40%-60% and median survival times of 8–11 months. However, there is no globally accepted standard regimen for the first-line treatment of advanced disease. Compared with ECE-D in combination with 5-FU c.i., capecitabine has shown a very interesting activity in a phase II randomised study (J Clin Oncol 23: 494; 2005). REAL-2 trial demonstrated that ECF, D in combination with 5-FU c.i. has shown a very interesting activity in the accepted standard regimen for the first-line treatment of advanced disease. Compared with ECF, D in combination with 5-FU c.i. has shown a very interesting activity in the accepted standard regimen for the first-line treatment of advanced disease. Compared with ECF, D in combination with 5-FU c.i. has shown a very interesting activity in the

Methods: Patients with previously untreated metastatic gastric adenocarcinoma, signed informed consent, evaluable lesion(s) by RECIST, ECOG 0-1, and adequate organ functions were eligible. Paclitaxel was given with 80mg/m² for 3-hour infusion on day 1, 5-FU with 1000mg/m² twice daily on day 1-2 (PF, 227) which was administered in 165 cases, CR and PR were achieved in 1.2% (2 cases) and 38.2% (63 cases) of patients (RR 39.4%), 75 patients had stable disease (45.5%), and 25 patients (15.1%) progressed. The disease control rate was 84.9%. After median follow-up of 11.4 months, 119 cases progressed and 87 cases died. Subsequent PFS was estimated by the Kaplan-Meier method. Median second time to progression (TTP) was 6.4 months in arm A versus 9.7 months in 37 patients treated by mFOLFIRI-4 followed by mFOLFOX-4. Median survival was 11.3 months in 40 patients treated by mFOLFOX 4 then radiotherapy in 7 pts and surgical excision in 10 with 6 R0 resection in 3 metastatic, 31/38 pts were PS 0 or 1; median age was 60 years (38-73); TFOX was administered as first line in 16 pts, in 2-3rd line in 22 pts. Efficacy level evaluation was made every 3 or 4 cycles according to the RECIST criteria.

Conclusion: PX-A as first-line treatment was promising in AGC. Based on the preliminary data of the phase II study, the phase III study (ML22697) has been launched for further investigation.

Disclosure: All authors have declared no conflicts of interest.

BIWEEKLY DOCETAXEL, FLUOROURACIL, LEUCOVORIN, OXALIPLATIN (TFOX) FOR ADVANCED GASTRIC AND OESOPHAGEAL ADENOCARCINOMA (AGEC): TOLERANCE AND RESPONSE IN 38 PATIENTS: PRELIMINARY REPORT

S. Perrin1, E. Metry1, C. Lecrem1, J.N. Valant1, M. El Hijazi2, C. Jule3, C. Lantuejoul4, B. Nordlinger5, P. Rougier6

1Fédération de Cancérologie Digestive, Hôpital Ambroise Pare´. Assistance Publique des Hôpitaux de Paris, Boulogne-Billancourt/FRANCE, 2Raiologie, Hôpital Ambroise Pare´. Assistance Publique des Hôpitaux de Paris, Boulogne-Billancourt/FRANCE

Introduction/Objectives: The Docetaxel-Capcitabin-SFU association is superior to 5-FU-Capcitabin in terms of response rate (RR) and overall survival (OS) in advanced gastric cancers, but is more toxic. We hypothesize that incorporating Docetaxel into a simplified FOLFOX regimen should be a tolerable and efficient option in AGEC.

Aims and Methods: The biweekly intravenous TFOX combining Docetaxel (50mg/m²), oxaliplatin (85mg/m²) on day 1, and 5FU continuous infusion of 480 (180mg/m²) administered every 2 weeks. Population: 38 patients (pts) with AGEC, 29 with gastric (6 limits plastica) and 9 oesophagal adenocarcinoma, locally advanced (n=17/38) or metastatic, (21/38); 31/38 pts were PS 0 or 1, median age was 60 years (38-73); TFOX was administered as first line in 16 pts in 2-3rd line in 22 pts. Efficacy level evaluation was made every 3 or 4 cycles according to the RECIST criteria.

Results: Mean number of cycles: 5.5 cycles (1-24), and 36% of pts received at least 4 cycles. Toxicity was evaluable in 32 pts; Overall Response Rate: 65.6% (n=21), Complete response (CR) in 4 pts (12.9%), partial response (PR) in 54.3% (15 pts) and stable disease in 44.6% (12 pts). Main toxicity rate (G3-4) in the evaluable patients assigned to TFOX was 30.6%, alopecia (22.8% versus 18.3%) and Hand-F syndrome (5.7% versus 0%). The worst toxicity (G3-4) in the arm A was anemia (9.6% versus 5.7%).

Conclusion: Our preliminary data suggest an higher ORR for ECF regimen when compared to DF with a favourable toxicity profile. Definitive data will be presented at the congress.

Disclosure: All authors have declared no conflicts of interest.
locally advanced and 3 R1 resection). Two pts with peritoneal carcinomatosis had a CR after TFOX and received intraperitoneal chemotherapy.

Tolerance of TFOX was good with no treatment-related deaths and 1 patient (3%) having a febrile neutropenia. The most frequent NCI-CTC grade 3 or 4 non-hematologic toxic effects was periperal neuropathy (19%) and diarrhea (10%).

Conclusion: These results showed that TFOX is effective and tolerable in AGC, it may facilitate secondary resection in initially non resectable cancer and should be evaluated in randomized studies. 

Disclosure: All authors have declared no conflicts of interest.

PHASE II STUDY OF WEEKLY PACLITAXEL, CISPLATIN, AND 5-FLUOROURACIL (PCF) FOR ADVANCED GASTRIC CANCER

K. Nishikawa1, T. Haru2, M. Sakakura2, K. Oba3, C. Abe4, J. Sakamoto5
1Surgery, Osaka General Medical Center, Osaka/JAPAN, 2Department of Surgery, Kousei Kauka Hospital, Takaoka/JAPAN, 3Surgery, Tanihama General Hospital, Tanihama/JAPAN, 4Translational Research and Clinical Trial Center Hokkaido University Hospital, Hokkaido University, Sapporo/JAPAN, 5JFPO Epidemiological and Clinical Research Information Network (ECCRN), Kyoto/JAPAN

Background: Our previous phase I study (Cancer Chemother Pharmacol. 2007, 59(S1-S6) provided evidence that combination chemotherapy with paclitaxel, cisplatin, and 5-fluorouracil (PCF) is effective and well tolerated in patients with advanced gastric cancer (AGC). 

Conclusions: The median TTF of 2nd line therapy alone was 112 days, while the median TTF of the 3rd line therapy (or more) was 231 days. The OS since the time of the 5+9 administration significantly correlated with the TTF of 5+9 (p<0.0063), while the OS since the 2nd line treatment administration (2nd OS) was independent of the TTF of 5+9.

Disclosure: All authors have declared no conflicts of interest.

RETROSPECTIVE STUDY REGARDING THE EFFICACY OF 2ND OR HIGHER LINE CHEMOTHERAPY OF PATIENTS IN ADVANCED OR RECURRENT GASTRIC CANCER (ARGC) AFTER THE FAILURE OF S-1 OR S-1 COMBINATION CHEMOTHERAPY (S+S)

K. Kubayashi1, A. Tsuji2, Y. Hata1, S. Morita3, T. Horii3
1Medical Oncology, Kochi Health Sciences Center, Kochi City/JAPAN, 2Radiology, Kochi Health Sciences Center, Kochi City/JAPAN, 3Digestive Surgery, Kochi Health Sciences Center, Kochi City/JAPAN

Results: Forty-two patients with ARGC who failed to sufficiently respond to S-1 underwent chemotherapy after S-1+9 therapy was 137 days. The 2nd-line treatment regimens included Taxanes; 30, CPT;11,11+S+P. The median number of 2nd or more treatment courses was 2 (1-5). The RR of 2nd line therapy was 14% (P=0.029, P<0.001). The median TTF of the 2nd-line chemotherapy was administered were 231 days and 345 days, respectively. The median TTF of 2nd-line chemotherapy alone was 112 days, while the median TTF of the 3rd line therapy (or more) was 231 days. The OS since the time of the 5+9 administration significantly correlated with the TTF of 5+9 (p<0.0063), while the OS since the 2nd line treatment administration (2nd OS) was independent of the TTF of 5+9.

Disclosure: All authors have declared no conflicts of interest.

SURVIVAL BENEFIT ASSOCIATED WITH FLUOROPYRIMIDINES, PLATINUM AGENTS, TAXANES, AND IRINOTECAN DURING ALL LINES OF TREATMENT IN PATIENTS WITH ADVANCED GASTRIC CANCER

K. Shiiba1, K. Matsuo2, D. Takahara3, T. Yokota1, T. Ura1, S. Itou1, A. Sawada1, M. Tajika1, H. Kawa1, K. Muro2
1Department of Clinical Oncology, Aichi Cancer Center Research Institute, Nagoya/JAPAN, 2Aichi Cancer Center Research Institute, Nagoya/JAPAN, 3Aichi Cancer Center Hospital, Nagoya/JAPAN

Background: Several agents were approved for AGC in Japan around 2000 (irinotecan in 1994, S-1 in 1999, oxaliplatin 2001, and capecitabine 2002). The three-drug regimen including capecitabine, oxaliplatin and irinotecan (COI) is an effective and well-tolerated upfront treatment for advanced colorectal cancer (Ann Oncol 2007; 18:1810-16). This dose contains some newer cytotoxic agents commonly used in the palliative treatment of AGC, we investigated the activity and safety of this combination regimen against gastric cancer.

Results: Forty-one consecutive patients (26 males and 15 females) who had a median age of 66 years (range, 41-74 years) were enrolled to receive the COI regimen. Six patients (14%) had locally advanced disease, and 16 patients (39%) retained the primary gastric lesion. Main disease sites included lymph nodes (41%), peritoneum (34%), and liver (21%). As present, 36 patients are assessable for response and toxicity. Five patients are still receiving chemotherapy before follow-up response assessment. A complete response was observed in 5 patients, and a partial response in 9 patients (ORR 38.9%, 95% CI 23.1-56.5%). Stable-disease occurred in 13 patients (36%). Analysis of both median time to progression and survival is still pending. Evaluable patients were treated with a median of six cycles (range, one to 8 cycles). The most common severe toxicities were grade 3 diarrhea and nausea that occurred in 32% and 25% of patients, respectively.

Disclosure: These preliminary data show that the COI regimen has activity as upfront therapy in fit patients with AGC, and it has a manageable toxicity. The ease of administration and good safety profile can make the COI regimen well suited for use as a platform for newer combinations with other biologic agents. (The authors would like to thank the I.T.M.O. service for data analysis.)

Disclosure: All authors have declared no conflicts of interest.
POTENTIALLY CURATIVE RESECTION BEFORE AND AFTER NEOADJUVANT CHEMOTHERAPY IN THE STOMACH OR GASTRO-ESOPHAGEAL JUNCTION (GEJ)

Methods: From 1994-2000, a total of 61 patients with resectable gastric cancer were analyzed. Peritoneal cytology was performed before NAC, at laparoscopy and at tumor resection. A minimum of six weeks of NAC, consisting of cisplatin, 5-fluorouracil and fluorouracil administered. FPTCs were detected immunohistochemically using Ber-EPA antibody.

Results: No FPTCs could be detected in 42 patients (69%), compared to 19 (31%) with FPTCs before NAC. During chemotherapy 40/42 patients (24%) developed FPTCs and 7/19 patients (37%) reverted from positive to negative. Patients who became FPTC negative (n=7) showed an improved median survival (36 months) and a longer 2-year survival (71.4%) compared to FPTC positive patients before and after NAC (n=12), with a median survival of 9.2 months and a 2-year survival rate of 25%. In contrast, patients who reverted from FPTC negative to positive during NAC (n=10) had a median survival of 18.5 months and a 2-year survival rate of only 20%. Multivariate analysis identified ypN category and FPTC change as independent prognostic factors.

Conclusions: NAC for patients with positive cytology could lead into FPTC negativity in a subset of patients and to improve their prognosis. However, NAC might be a risky strategy for almost one-quarter of patients who develop positive cytology.

Disclosure: All authors have declared no conflicts of interest.

PHASE II STUDY OF TELATINIB IN COMBINATION WITH CAPETIBABINE AND CISPLATIN AS FIRST-LINE TREATMENT IN PATIENTS WITH ADVANCED CANCER OF THE STOMACH OR GASTRO-ESOPHAGEAL JUNCTION (GEJ)

Methods: Fifty-four patients were enrolled between July 2008 and February 2010. Dosing was given until disease progression or unacceptable toxicity. Primary endpoint was to determine 4-month progression-free survival (PFS) and secondary end points were to investigate response rate, toxicity and overall survival (OS) rate.

Results: In addition to FP, 19 patients were refractory to docetaxel and two failed irinotecan, respectively. A total of 180 cycles of everolimus were administered with a median of 2 (range, 1-20) cycles in each patient. Two patients (3.7%) achieved confirmed partial response and 19 patients (35.2%) showed stable disease, resulting in a disease control rate of 38.9%. A median follow-up duration of 8.7 months in surviving patients (range, 3.0 – 19.4 months), a 4-month PFS rate was 18.4% with a median PFS of 1.7 months (95% confidence interval [CI], 1.5-2.2 months) and a median OS time was 8.5 months (95% CI, 4.5-12.1 months). Peritoneal metastasis was significantly associated with shorter PFS time (Hazard ratio, 3.97; 95% CI, 1.54-10.23; p=0.010). Treatment was in general well tolerated. Grade 3/4 anemia and dyslipidemia occurred in 6 patients (asymptomatic in 4, death in 1). Grade 3 hypertension or hand-foot syndrome occurred in <5% of patients. 12% of patients discontinued study treatment due to tel related AEs.

Conclusion: Tel-XP resulted in rapid disease control within 2 cycles, with substantial antitumor responses that appear durable. The combination was well tolerated, and does not appear to increase toxicity substantially compared to the doublet chemotherapy alone. The drug profile allows continuous inhibition of angiogenesis without increase in off target toxicities.

Disclosure: All authors have declared no conflicts of interest.

PROGNOSTIC SIGNIFICANCE OF FREE PERITONEAL TUMOR CELLS (FPTCS) IN THE PERITONEAL CAVITY BEYOND THE ADVANCED STAGE OF GASTRIC CANCER PATIENTS TREATED WITH ADJUVANT CHEMOTHERAPY INCLUDING FLUOROPYRIMIDINE AND PLATINUM

Methods: Fifty-four patients were enrolled between July 2008 and February 2010. Dosing was given until disease progression or unacceptable toxicity. Primary endpoint was to determine 4-month progression-free survival (PFS) and secondary end points were to investigate response rate, toxicity and overall survival (OS) rate.

Results: In addition to FP, 19 patients were refractory to docetaxel and two failed irinotecan, respectively. A total of 180 cycles of everolimus were administered with a median of 2 (range, 1-20) cycles in each patient. Two patients (3.7%) achieved confirmed partial response and 19 patients (35.2%) showed stable disease, resulting in a disease control rate of 38.9%. A median follow-up duration of 8.7 months in surviving patients (range, 3.0 – 19.4 months), a 4-month PFS rate was 18.4% with a median PFS of 1.7 months (95% confidence interval [CI], 1.5-2.2 months) and a median OS time was 8.5 months (95% CI, 4.5-12.1 months). Peritoneal metastasis was significantly associated with shorter PFS time (Hazard ratio, 3.97; 95% CI, 1.54-10.23; p=0.010). Treatment was in general well tolerated. Grade 3/4 anemia and dyslipidemia occurred in 6 patients (asymptomatic in 4, death in 1). Grade 3 hypertension or hand-foot syndrome occurred in <5% of patients. 12% of patients discontinued study treatment due to tel related AEs.

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Disclosure: All authors have declared no conflicts of interest.

HELICOBACTER PYLORI INFECTION AS AN INDEPENDENT PROGNOSTIC FACTOR FOR LOCALY ADVANCED GASTRIC CANCER PATIENTS TREATED WITH ADJUVANT CHEMOTHERAPY AFTER CURATIVE RESECTION

Methods: From 1994-2000, a total of 61 patients with resectable gastric cancer were analyzed. Peritoneal cytology was performed before NAC, at laparoscopy and at tumor resection. A minimum of six weeks of NAC, consisting of cisplatin, 5-fluorouracil and fluorouracil administered. FPTCs were detected immunohistochemically using Ber-EPA antibody.

Results: No FPTCs could be detected in 42 patients (69%), compared to 19 (31%) with FPTCs before NAC. During chemotherapy 40/42 patients (24%) developed FPTCs and 7/19 patients (37%) reverted from positive to negative. Patients who became FPTC negative (n=7) showed an improved median survival (36 months) and a longer 2-year survival (71.4%) compared to FPTC positive patients before and after NAC (n=12), with a median survival of 9.2 months and a 2-year survival rate of 25%. In contrast, patients who reverted from FPTC negative to positive during NAC (n=10) had a median survival of 18.5 months and a 2-year survival rate of only 20%. Multivariate analysis identified ypN category and FPTC change as independent prognostic factors.

Conclusions: NAC for patients with positive cytology could lead into FPTC negativity in a subset of patients and to improve their prognosis. However, NAC might be a risky strategy for almost one-quarter of patients who develop positive cytology.

Disclosure: All authors have declared no conflicts of interest.

HELICOBACTER PYLORI INFECTION AS AN INDEPENDENT PROGNOSTIC FACTOR FOR LOCALY ADVANCED GASTRIC CANCER PATIENTS TREATED WITH ADJUVANT CHEMOTHERAPY AFTER CURATIVE RESECTION

Methods: From 1994-2000, a total of 61 patients with resectable gastric cancer were analyzed. Peritoneal cytology was performed before NAC, at laparoscopy and at tumor resection. A minimum of six weeks of NAC, consisting of cisplatin, 5-fluorouracil and fluorouracil administered. FPTCs were detected immunohistochemically using Ber-EPA antibody.

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EXPRESSION OF BAX PREDICTS OUTCOME IN ADVANCED GASTRIC CANCER PATIENTS TREATED WITH 5-FUOROURACIL AND PLATINUM PALLIATIVE CHEMOTHERAPY
S.H. Jeong, S.Y. Kang, J.H. Choi
Hematology-Oncology, Ajou University School of Medicine, Suwon/SOUTH KOREA

Purpose: The present study evaluated the predictive role of Bax, excision repair cross-complemented group 1 (ERCC1), and thymidylate synthase (TS) on clinical outcomes in patients with advanced gastric cancer treated with 5-fluorouracil (5-FU) and platinum palliative chemotherapy.

Materials and methods: One hundred and twenty-eight patients with metastatic or recurrent gastric cancer were treated with a chemotherapy regimen of either 5-FU and leucovorin, or oxaliplatin (FOLFOX) (72 patients). Pretreatment tumor biopsy specimens were analyzed for Bax, ERCC1, and TS expression by immunohistochemistry (IHC).

Results: High expression of Bax, ERCC1 and TS was observed in 49 (38%), 60 (47%), and 48 (38%) patients, respectively. The median overall survival (OS) of patients in total was 10 months. Low expression of Bax was associated with poor OS (median; 9 months vs. 12 months; 2-year; 7% vs. 32%; P=0.0005) in univariate analysis, while expression of ERCC1 and TS was not correlated with patient outcome. The expression of low expression of Bax was significantly worse in the FOLFOX group (median OS; 9 months vs. 18 months; P=0.0008), without significant difference in the FH group. In multivariate analysis, low expression of Bax was a significant independent predictor of poor OS (P=0.014).

Conclusions: Low expression of Bax was significantly associated with the poor survival of patients with metastatic or recurrent gastric cancer treated with 5-FU and platinum chemotherapy. Immunohistochemical staining for Bax with pretreatment biopsy specimen may be useful in selecting FOLFOX regimen as a treatment option for these patients.

Disclosure: All authors have declared no conflicts of interest.

728P

MICRORNA-196B AND MICRORNA-363 WERE IDENTIFIED AS GASTRIC CANCER SPECIFIC MICRORNAs IN HUMAN GASTRIC CANCER TISSUE USING MICROARRAY EXPERIMENT
J.Y. Choi1, J.Y. Lim2, S. Kimm3, Y. Park4, J. Lee5
1Medical Oncology, Gangnam Severance Hospital, Gang Nam, Seoul/SOUTH KOREA, 2Systems Biology, UT MD Anderson Cancer Center, Houston/TX/UNITED STATES OF AMERICA

Background: MicroRNAs regulate gene expression post-transcriptionally by degradation or inhibition of translation of target mRNA through which regulate cell proliferation and apoptosis, and play a role in the pathogenesis of various human cancers. Here we investigated gastric cancer specific microRNAs in human gastric cancer samples.

Method: We performed microRNA microarray experiments in 60 fresh frozen gastric cancer samples and 8 normal surrounding tissues. Total RNA was extracted and microarray experiments were performed according to the manufacturer’s protocols. The microarray data were normalized. Gastric cancer specific microRNAs were extracted through two tailed t-test (p<0.01). The obtained results were validated with quantitative reverse transcription-PCR in another paired 12 patients samples. MiRecords (http://mirecords.umn.edu/miRecords) was used as bioinformatics tools for screening predicted miRNA target genes. The results were combined with gene expression microarray data which came from same patient samples.

Results: 19 microRNAs were highly expressed (>2-fold change) in gastric cancer tissue and 18 were regulated (<0.5 fold change) compared to non-cancer tissue. Out of 37 gastric cancer specific microRNAs, four microRNAs including miR-135b, miR-196b, miR-363, and mir-193a-3p were validated by quantitative reverse transcription-PCR. miR-196b and miR-363 showed statistically significant results (p = 0.007 and 0.0001, respectively) in two sample paired t-test. Common genes which expression were negatively correlated with microRNA expression (Pearson correlation, r=−0.05) and also identified as predicted targets using microRNA target searching programs were regarded as target gene candidates in specifically gastric cancer. Using this method, we could identify 265 and 74 target genes of miR-196b and miR-363, respectively.

Conclusions: MiR-196b and miR-363 were revealed as gastric cancer specific microRNAs using microarray experiment. Among target candidate genes of these microRNAs, ADAM15 was most reliable target gene of miR-363. It is worthy to validate the relation of ADAM15 and stage III or stage IV gastric cancer.

Disclosure: All authors have declared no conflicts of interest.

729P

MRNA EXPRESSION OF BRCA1, RPAP6 AND SUMO LIGASES (PIAS1 AND PIAS4) AND SURVIVAL IN GASTRIC CANCER PATIENTS (P) RECEIVING SECOND-LINE DOCETAXEL (DOC)
J. Wei1, C. Costa2, Z. Zou1, L. Yu3, H. Chen1, X. Qian1, E. Liu1, S. Benlloch3, M. Piro2, R. Rosell1
1Cancer Center, Affiliated Drum Tower Hospital, Medical School of Nanjing University, Nanjing/CHINA, 2Oncology, Pangea Biotech, USP Deusto University Institute, Barcelona/SPAIN, 3Medical Oncology Service, Institut Català d’Oncologia, Badalona/Barcelona/SPAIN

Background: BRCA1 and RPAP6 are implicated in response to chemotherapy, and SUMO pathway components (PIAS1, PIAS4) are required in DNA damage repair. PIAS1 influences BRCA1 and RPAP6 accumulation, and PIAS4 is involved earlier in DNA damage response. The involvement of the SUMO pathway in DNA damage response could mean that alterations of SUMOylated proteins could have a dramatic response on chemotherapy response.

Methods: We have examined the expression of BRCA1, RPAP6, PIAS1 and PIAS4 by RT-QPCR in 133 advanced gastric cancer patients treated with FOLFOX, 59 of whom received second-line doc.

Results: Median age: 74 p not receiving doc, 64 years; 59 receiving doc, 58 years (P=0.15). No other differences in baseline characteristics were observed. 102 males; 41 stage IIIA, 41 stage IIIB, 31 stage IV. A good correlation between the expression of the four genes was observed (P<0.001). Median survival (MS) was 12.5 months (m) overall. For the 59 p receiving doc, MS was 24.8 m for p with high BRCA1 levels and 9.5 m for p with low BRCA1 (P=0.002), 19.1 m for p with high PIAS4 and 8.5 for p with low PIAS4 (P=0.03). In the multivariate analysis, shorter MS was seen in p not receiving second-line doc (HR, 1.82; P=0.01) and in stage IV p (HR, 2.63; P=0.002), and longer MS was seen in p with high PIAS1 levels (HR, 0.45; P=0.004).

Conclusions: Alterations in BRCA1 SUMOylation could predict outcome to chemotherapy. Trials of customized chemotherapy based on the levels of BRCA1 and PIAS4 could help to optimize treatment in gastric cancer p.

Disclosure: All authors have declared no conflicts of interest.

730P

SUVMAX OF F-18 FDG-PET/CT IN ADVANCED GASTRIC CANCER WITH TUBULAR ADENOCARCINOMA: CORRELATION WITH PATHOLOGIC FINDINGS INCLUDING IMMUNOHISTOCHEMICAL STAINING
1Hematology-Oncology, Dongsan Medical Center, Daegu/SOUTH KOREA, 2Nuclear Medicine, Dongsan Medical Center, Daegu/SOUTH KOREA, 3Pathology, Dongsan Medical Center, Daegu/SOUTH KOREA, 4Internal Medicine, Daeug Fatima Medical Center, Daegu/SOUTH KOREA, 5Internal Medicine, Daeug Catholic Univ Medical Center, Daegu/SOUTH KOREA

Background: The role of F-18 FDG PET-CT in gastric cancer is limited because of its low sensitivity, which ranges from 78% to 93% in advanced gastric cancer (AGC). This retrospective study was designed to assess the accuracy of F-18 FDG PET-CT in AGC with tubular adenocarcinoma and its correlation with other pathologic findings including immunohistochemical staining.

Methods: One hundred and fifty two patients with AGC (age:60±10.4 years, M:F=106:46) who underwent F-18 FDG PET-CT in 1 month before operation were included for this study. They were divided into 3 groups according to the SUVmax of the tumor. All patients were reviewed medical records including immunohistochemical staining results. All parameters were compared among 3 groups by one-way ANOVA and 2-test.

Results: The mean SUVmax was 8.19 in AGC with tubular adenocarcinoma. Group 1 was 62 patients with tumor SUVmax lower than 5, group 2, 53 patients with SUVmax 5.0-9.9 and group 3, 37 patients with SUVmax 10.0. The intensity of FDG uptake was correlated with tumor size (r²=0.352, p<0.001) and GLUT1 expression (r²=0.225, p<0.006). The intensity of FDG uptake showed significant difference with T stage, N stage, GLUT1 expression, and Ming and Lauren classification. SUVmax was higher in expanding type of Ming and intestinal type of Lauren. And all of the immunohistochemical parameters including p53, Ki-67, C-erbB-2, Rh, EGFR and tumor differentiation were not related to the degree of SUVmax.
Conclusions: Preoperative tumor SUVmax of F-18 FDG-PET/CT in AGC with tubular adenocarcinoma was correlated with tumor size, T and N stage, GLUT-1 expression and Ming and Lauren classification.

Disclosure: All authors have declared no conflicts of interest.

**731P** PREDICTIVE FACTORS FOR ADJUVANT THERAPY IN PATIENTS WITH LOCALIZED GASTRIC AND GASTRO-ESOPHAGEAL JUNCTION (G/GEJ) CANCER: A POPULATION-BASED STUDY

S. Ahmed1, T. Zhu2, K. Haider2, F. Arneko3, S. Yadav2, C. Woitas2, A. Amjad4, K. Haider3, F. Arnold3, S. Yadav3, C. Woitas2, A. Amjad4

1Medical Oncology, Saskatoon Cancer Center, University of Saskatchewan, Saskatoon/CANADA, 2Radiation Oncology, Allan Blair Cancer Center, Regina/CANADA, 3Hematology-oncology, Medicine, Gachon University Gil Hospital, Incheon/SOUTH KOREA, 4Radiation Oncology, Allan Blair Cancer Center, Regina/CANADA

Background: Adjuvant chemo-radiation therapy (CRT) results in significant improvement in survival of patients with high risk gastric and gastro-esophageal junction (G/GEJ) cancer. Little is known about the predictive factors of adjuvant CRT in such patients. Our study aims to determine predictive markers for adjuvant CRT in patients with localized G/GEJ cancer and to identify that factors correlate with survival.

Methods: Medical records of patients with localized G/GEJ cancer diagnosed between 2002 and 2007 in the province of Saskatchewan were reviewed. Logistic regression analysis was done and various clinicopathological factors were examined to identify predictive markers for adjuvant CRT. A Cox proportional hazards models was done to determine prognostic markers with respect to survival.

Results: 162 eligible patients with median age of 70 yrs and M:F of 65:35 were identified. 51% patients had ECOG PS of 0. 66% patients had gastric cancer, 54% had stage IB and II disease and 37% had node negative disease. Of 162 patients 34% received adjuvant CRT. Of 102 patients who did not receive adjuvant CRT, 32% patients were referred for CRT, 44% patients were not found to be optimal candidate, and 24% declined adjuvant CRT. On multivariate analysis positive resection margin (HR 2.9; 95% CI: 1.0-8.4), stage 3 and 4 disease (HR 2.4; 95% CI: 1.1-5.2), and grade tumor (HR 2.5; 95% CI: 1.0-5.0) were correlated with adjuvant CRT. Median survival of patients who received adjuvant CRT was 32 months compared with 22 months of patients who did not received CRT (p=0.09). On multivariate analysis node negative disease (HR 0.35; 95%CI: 0.17-0.72), adjuvant CRT (HR 0.38; 95%CI: 0.22-0.66), R0 resection (HR 0.51; 95%CI: 0.28-0.92), and ECOG PS 0 (HR 0.52; 95%CI: 0.32-0.84) correlated with a superior survival.

Conclusions: Nearly two third patients did not receive adjuvant therapy. Half of the patients were not referred or declined adjuvant therapy. Positive resection margin, stage 3 and 4 disease, and high grade tumor were identified as predictive markers for adjuvant therapy. ECOG PS, adjuvant therapy, resection margin and lymph node status correlated with prognosis in such patients.

Disclosure: All authors have declared no conflicts of interest.

**734P** PROGNOSTIC IMPACT OF IMMUNOHISTOCHEMICAL EXPRESSION OF KI-67 IN PATIENT WITH ADVANCED GASTRIC CANCER WHO UNDERWENT CURATIVE RESECTION


1Internal Medicine, Gachon University Gil Hospital, Incheon/SOUTH KOREA, 2Hematology and Oncology, Internal Medicine, Gachon University Gil Medical Center, Incheon/SOUTH KOREA, 3General Surgery, Gachon University Gil Medical Center, Incheon/SOUTH KOREA, 4Pathology, Gachon University Gil Medical Center, Incheon/SOUTH KOREA

Background: Ki-67, proliferation marker, in an important prognostic factor in a variety of cancers. In the present study, we investigated the prognostic value of immunoeexpression of Ki-67 in patient with gastric cancer who underwent curative resection.

Material and methods: We retrospectively analyzed 241 patients who had undergone curative gastrectomy at Gachon University Gil Hospital between January 2008 and July 2009. Ki-67 proliferation index (PI) by immunohistochemistry on formalin-fixed, paraffin-embedded material and the other clinicopathologic variables were evaluated by univariate and multivariate analysis.

Results: The median follow-up from surgery was 12 months (range, 0.5-26.7 months) and mean recurrence-free survival was 23 months (95% confidence interval, 21-24.1 months). The mean Ki-67 PI was 48% (range, 5-90%). No significant correlation was found between Ki-67 PI and other clinicopathologic variables including histologic grade and pathologic T stage. Multivariate analysis revealed that significant prognostic factors were recurrence-free survival included age, pre-operative albumin, pre-operative hemoglobin, surgery type, pTNM, histologic grade, lymphatic vessel invasion, peri-neural invasion, and Ki-67 PI. In the multivariate analysis besides pTNM (p=0.046), lymphatic vessel invasion (p=0.024), and surgery type (p=0.047), Ki-67 PI (p=0.005) also remained as an independent prognostic factor of recurrence, whereas the other factors lost its prognostic value.

Conclusions: Our results suggested that high Ki-67 PI was independent, poor prognostic factor of recurrence in patient with gastric cancer who underwent curative resection.

Disclosure: All authors have declared no conflicts of interest.

**735P** PREDICTIVE SIGNIFICANCE OF PREOPERATIVE PERIPHERAL BLOOD VOLUMES FOR STAGE IV GASTRIC CANCER

M. Aizawa, N. Gotohida, Y. Kato, S. Takahashi, M. Korieh, T. Kinoshita

Upper Abdominal Surgery, National Cancer Center Hospital East, Kawasaki/JAPAN

Background: The preoperative diagnostic accuracy of gastric cancer staging is defined deeper wall invasion than muscularis propria (T2/T3). Patients receiving neoadjuvant chemotherapy were excluded. T stage and nodal status were compared to preoperative hematological and biochemical parameters. Subsequently the predictive value for stage T4 was evaluated by multiple logistic regression analysis.

Result: In total of 304 cases, the median age was 64 years old, 209 (68.8%) were male and 95 (31.2%) were female. All was estimated indication to curative resection before surgery. The curative resection was accomplished in 264 (86.8%) whereas the distant metastasis was diagnosed on laparotomy in 40 (13.2%). Depth of primary lesion was assessed as stage T2 in 78 (25.7%), stage T3 in 127 (41.8%) and stage T4 in 99 (32.6%). Elevated neutrophil/lymphocyte (N/L) ratio, platelet/lymphocyte (P/L) ratio and serum CRP and decreased lymphocyte count, hemoglobin, serum total protein and serum albumin were significantly correlated with stage T4 respectively. Odds ratio for N/L (OR=1.192 95%CI, 1.034-1.343, p=0.019) and serum CA19-9 (OR=2.927 95%CI, 1.429-5.997, p=0.003) were suggested significant predictive values for stage T4.

Conclusion: Preoperative values of N/L and serum CA19-9 may be reliable factors to assess preoperative staging in advanced gastric cancer.

Disclosure: All authors have declared no conflicts of interest.

**SURVIVAL BENEFIT OF GASTRECTOMY ± METASTASECTOMY IN METASTATIC GASTRIC CANCER PATIENTS RECEIVING CHEMOTHERAPY**

K.H. Kim1, K. Lee1, S.K. Bae1, H.J. Chang1, Y.J. Kim1, D.J. Park2, J.H. Kim1, H. Kim1, J.S. Lee1

1Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam-Si/SOUTH KOREA, 2Department of Surgery, Seoul National University Bundang Hospital, Seongnam-Si/SOUTH KOREA

Background and Objectives: To investigate the role of surgery in gastric cancer (GC) with distant metastasis.

Methods: Newly diagnosed 274 GC patients with synchronous metastases who had received chemotherapy were categorized into 3 groups according to applied surgical treatment: complete gross resection of both primary and metastatic sites (group A, n = 42), debulking gastrectomy (group B, n = 47) and chemotherapy without debulking (group C, n = 185).

Results: Median overall survival (OS) of all patients was 11.8 months. Median OS and 3-year survival rate were 28.0, 15.5 and 9.0 months and 42.8%, 8.1% and 3.5% in groups A, B and C, respectively. In group A, patients with peritoneal seeding, intra-abdominal distant lymph nodes, ovarian or hepatic metastases underwent complete gross resection and 12 (28%) had no evidence of recurrence at the time of last analysis (median follow-up duration, 29.1 months). In multivariate analysis, the adjusted hazard ratios for death were calculated at 0.23 (p = 0.011) and 0.27 (p = 0.012) in group A and C, respectively. Furthermore, the 3-year OS rate was 59.3% and 32.9% in group A and C, respectively.

Conclusions: We found a significant survival benefit of debulking gastrectomy or gastrectomy plus metastasectomy in GC patients with distant metastasis.

Disclosure: All authors have declared no conflicts of interest.

**10-YEAR FOLLOW-UP OF GASTRIC SUBMUCOSAL TUMORS**


1Oncology, Aichi Cancer Center Hospital, Nagoya/JAPAN, 2Gastroenterology, Aichi Cancer Center Hospital, Nagoya/JAPAN, 3Endoscopy, Aichi Cancer Center Hospital, Nagoya/JAPAN

Background: Gastric submucosal tumors (SMTs) were incidentally discovered by endoscopic or radiological examination. However, they have not been studied in detail of epidemiology or treatment strategy for SMTs. The aim of this study is to clarify the clinical features and long-term outcomes of gastric SMTs.

Methods: A data base was established by endoscopic medical records from January to December 1998 in Aichi Cancer Centre. All clinical data of gastric SMTs were collected.
RESULTS: We performed 5307 EGDs and detected 188 gastric SMTs (3.5%; 81 males, 107 females) during one year. Majority of SMTs was less than 1cm (64%) and SMTs<2cm were equally detected at upper (22%) and lower (22%), respectively. Sixteen SMTs were >2cm and fifteen were monitored for 10 years. 4 cases underwent surgery because two (leiomyosarcoma) was ≥2cm, one (GIST) enlargement and one (GIST) simultaneously resected with gastrectomy for gastric cancer. One leiomyosarcoma appeared liver metastases. 172 SMTs were <2cm and 156 followed for ten years. Three SMTs were enlarged: two underwent surgery and one followed because enlarged size was <1cm. Two resected SMTs were GIST and one of them was recurred. Observed pts <2cm were detected no SMT related death.

CONCLUSIONS: The incidence of SMT is 3.5%, majority (91%) is small (<2cm), and frequent location is middle one third of stomach. Large size (>2cm) and enlargement was <1cm. Two resected SMTs were GIST and one of them was recurred. Observed pts <2cm were detected no SMT related death.

Disclosure: All authors have declared no conflicts of interest.

COST-EFFECTIVENESS OF ADJUVANT IMATINIB IN PATIENTS WITH SURGICALLY RESECTED LOCALIZED GASTROINTESTINAL STROMAL TUMOR (GIST): A CANADIAN SOCIETAL PERSPECTIVE

V. Pawar1, K. El Ouagai2, J. Rubin1, J.H. Coombs3, D. Taylor1

1Health Economics and Outcomes, I3 Innovus, Medford/MA/UNITED STATES OF AMERICA, 2Health Economics and Pricing, Novartis Pharmaceuticals Corp,, Florham Park/UNITED STATES OF AMERICA, 3Novartis Oncology, Florham Park/UNITED STATES OF AMERICA

Background: Treatment with adjuvant imatinib following surgical resection of localized GIST has been shown to increase recurrence-free survival (RFS) compared with surgical resection alone (SRA) in patients who are at intermediate to high risk of relapse. The objective of this study was to evaluate the cost-effectiveness of treatment with adjuvant imatinib in Canada.

Methods: A lifetime Markov model predicts patients’ transitions across health states defined by initial treatment (adjuvant imatinib versus SRA). Recurrence rates are based on data from the ACOGOG Z9001 study. Two scenarios were evaluated: (1) 1-year scenario where 1-year trial results were used to calculate first year recurrence rates for imatinib and SRA. For subsequent years of the model the recurrence rate for imatinib was set equal to SRA and, (2) continuous scenario where recurrence rates for imatinib and SRA at the end of one year are continued over the lifetime. The model estimates direct and indirect costs (loss earnings due to early mortality and short-term disability), life-expectancy, quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios (ICER). Results are from the societal perspective in $2009 Canadian and discounted at 5% per annum. Deterministic and probabilistic sensitivity analyses (Dx and PSA) were performed to assess the impact of parameter uncertainty on model results.

Results: Adding imatinib was estimated to result in a gain of 0.745 and 5.180 QALYs at an additional expected per-patient lifetime cost of $26,800 and $326,000 for the 1-year and continuous treatment scenarios, respectively. Corresponding ICERs per QALY were therefore $60,000 and $63,000. In the Dx, model results were most sensitive to recurrence rates. Overall, results remained consistent in the PSA; 95% CI for ICERs were $31,600 to $39,400 for the 1-year and $60,400 to $65,000 for the continuous treatment scenario.

Conclusions: Results of this evaluation suggest that, from a Canadian health care system perspective, imatinib is cost-effective and represents good value for the money according to currently accepted standards of cost effectiveness.


PATIENT PREFERENCES FOR REDUCING TOXICITIES OF TREATMENTS FOR GASTROINTESTINAL STROMAL TUMOR (GIST): A CONJOINT ANALYSIS STUDY

J.M. Gonzalez1, B. Hauber1, J.H. Coombs2, A. Shrik1, D. Palacios1, N. Scherzer3
1Health Solutions, Research Triangle Institute, Research Triangle Park/NC/UNITED STATES OF AMERICA, 2Health Economics and Pricing, Novartis Oncology, Florham Park/UNITED STATES OF AMERICA, 3Novartis Pharmaceuticals, East Hanover/UNITED STATES OF AMERICA

Objectives: To quantify GIST patients’ preferences for reducing treatment toxicities and the likely effect of toxicities on patients’ stated adherence.

Methods: English-speaking members of the Life Raft Group, a GIST patient advocacy and research organization, aged 18 years and over completed a web-enabled survey that presented a series of treatment-choice questions, each including a pair of hypothetical GIST medication toxicity profiles. Each profile was defined by common or concerning toxicities verified via pre-test interviews including: severity of edema, diarrhea, nausea, fatigue, rash, hand-foot syndrome, and heart failure, or risk of serious infection. Each subject answered 13 choice questions based on predetermined experimental design with known statistical properties. Subjects were asked to rate the likelihood that they would miss or skip doses of medications with different toxicity profiles. Random-parameters logit was used to estimate a relative preference weight for each level of each toxicity. The study underwent IRB review and approval and subjects provided informed consent.

Results: 175 subjects completed the survey. Over the ranges of attribute levels included in the study, heart failure was the most important attribute and was assigned an importance weight of 10. Relative to heart failure, remaining attributes were ranked in order of importance.

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Importance Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure</td>
<td>10.0</td>
</tr>
<tr>
<td>25% chance of serious infection</td>
<td>6.8</td>
</tr>
<tr>
<td>Nausea</td>
<td>5.8</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4.8</td>
</tr>
<tr>
<td>Hand-foot syndrome</td>
<td>4.3</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3.4</td>
</tr>
<tr>
<td>Rash</td>
<td>3.3</td>
</tr>
<tr>
<td>Edema</td>
<td>3.1</td>
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</tbody>
</table>

For all attributes, reducing severity of toxicities from severe to moderate was more important to subjects than reducing severity from moderate to mild. Reducing heart failure from moderate to mild and diarrhea from severe to moderate had the largest effects on subjects’ evaluation of adherence.

Conclusions: All toxicities and risks included in the study are important to patients. Treating or reducing severe toxicities is much more important to GIST patients than treating or reducing moderate toxicities. Focused reductions of certain toxicities may improve treatment adherence.

Disclosure: J.H. Coombs: This study was funded by Novartis. John Coombs is an employee of Novartis. A. Shrik: This study was funded by Novartis. Andres Shrik is an employee of Novartis. D. Palacios: This study was funded by Novartis. David Palacios is an employee of Novartis. All other authors have declared no conflicts of interest.
**Abstract: 741P**

<table>
<thead>
<tr>
<th>COX + Gem (Arm 1)</th>
<th>AMG 479 + Gem (Arm 2)</th>
<th>Pbo + Gem (Arm 3)</th>
<th>Arm 1 vs 3</th>
<th>Arm 2 vs 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-mo OS (95% CI)*</td>
<td>59% (42, 73)</td>
<td>57% (41, 70)</td>
<td>50% (33, 64)</td>
<td>10% (-12, 31)</td>
</tr>
<tr>
<td>12-mo OS (95% CI)</td>
<td>20% (9.34)</td>
<td>39% (25, 34)</td>
<td>23% (11, 38)</td>
<td>-3% (-23, 16)</td>
</tr>
<tr>
<td>OS events</td>
<td>32% (98%)</td>
<td>29% (69%)</td>
<td>34% (81%)</td>
<td>3% (19, 58)</td>
</tr>
<tr>
<td>Median OS (95% CI), mo</td>
<td>7.5 (4.8, 10.0)</td>
<td>8.7 (5.3, 12.2)</td>
<td>5.9 (4.1, 9.7)</td>
<td>HR = 0.87 (0.53, 1.43); p = 0.59</td>
</tr>
<tr>
<td>PFS events</td>
<td>38% (93%)</td>
<td>37% (88%)</td>
<td>38% (90%)</td>
<td>-</td>
</tr>
<tr>
<td>Median PFS (95% CI), mo</td>
<td>4.0 (3.3, 5.0)</td>
<td>5.1 (2.8, 5.8)</td>
<td>2.1 (1.9, 3.3)</td>
<td>HR = 0.65 (0.41, 1.05); p = 0.08</td>
</tr>
<tr>
<td>Objective response</td>
<td>1/38 (3%)</td>
<td>4/39 (10%)</td>
<td>1/38 (3%)</td>
<td>-</td>
</tr>
<tr>
<td>Stable disease</td>
<td>22/38 (58%)</td>
<td>16/39 (41%)</td>
<td>15/40 (38%)</td>
<td>-</td>
</tr>
</tbody>
</table>

*Primary endpoint. Data cut off, March 2010.*
received CON 10 mg/kg, AMG 479 12 mg/kg, or pbo IV days (D) 1 and 15 and gem 1000 mg/m2 IV on 30 min D 1, 8, 15 Q 28 D. Randomization was stratified by PS (0 vs 1). CT scans were done Q 2 cycles. Primary endpoint: 6-month (mo) overall survival (OS). 125 pts (Arms 1/2/3: 41/42/42 pts) enrolled between 3/08 and 4/09. 4/40/40 received (21) dose of study drug. Median age, 61/66/62 years; male, 59/60/52%; PS 1, 59/55/62%; liver metastases, 66/69/79%. Summary: CON + gem or AMG 479 + gem was well tolerated in this pt population. AMG 479 + gem vs pbo + gem trended toward improved 6-mo OS (57% vs 50%), 12- mo OS (39% vs 23%), median OS (12.7 vs 9.4 mo), and median PFS (5.1 vs 2.1 mo). These data suggest that further study of AMG 479 + gem is warranted in advanced PC. Efficacy Disclosure: H. Kindler: Consultant/advisory to Amgen, Clovis, BMS, Merck, Roche, Abbott, Genentech. J. Stephenson and C. Rocha Lima: Research funding from Amgen H. Kindler: Consultant/advisory: Amgen, Clovis, BMS, Merck, Roche, J. Im: Consultant: Amgen, Clovis, BMS, Merck, Roche, NEI, Merck, Abbott, Genentech, Merck, Theralogix. J. M. Oortgiesen1, L.A. Dimichele2, J.R. Weidman3, T. Soeder2, A. Cato2, L.Y. Sutton2

Background: Gastrin hormone is trophic to in vitro pancreatic cancer, and antigastrin antibodies (AGAs) are antiproliferative and antimetastatic. Human pancreatic cancers overexpress gastrin genes and receptors that react to gastrin's trophic effects. Polyclonal Antibody Stimulator (PAS) elicits a specific and high-affinity AGA. Methods: In this randomized, double-blind, placebo controlled, group sequential trial, patients received PAS vaccination or placebo intramuscularly on Weeks 0, 1, 3, and 24. Eligible patients had historically or cytologically confirmed pancreatic adenocarcinoma (unsuitable for curative resection) with a life expectancy >2 months. The primary endpoint of the study was overall survival (OS). Results: Adult patients with Stage II, III, or IV pancreatic carcinoma were randomized; all patients were included in the intent-to-treat (ITT) analyses of efficacy, demography and baseline characteristics. 154 patients - 79 on PAS and 75 on placebo. In the ITT population, survival was significantly longer for the PAS group than for the placebo group (median 150 days vs 84 days, respectively; p=0.016). Secondary endpoints, e.g., Quality of Life, performance status and weight, confirmed clinical benefit in PAS treated patients. In the PAS arm, 49 patients (64.5%) mounted measurable AGAs. AGA responsiveness was positively associated with survival, a covariate independent of baseline health status. Except for injection site reactions, PAS did not have an adverse effect on safety. Conclusions: The results demonstrated that successful treatment with PAS prolongs survival and may inhibit tumor progression, as would be expected with cytostatic therapy. Further, PAS is safe and very well tolerated in the context of cancer therapies. AGA response was an independent OS prognosticator; the analysis of survival time between patients mounting measurable AGAs and those who did not using Kaplan-Meier estimates shows statistically significant results between the patient groups. PAS provides a new therapeutic option for patients with advanced pancreatic cancer who may not be suitable for or refuse cytostatic chemotherapy.

Disclosure: J.M. Oortgiesen, L.A. Dimichele, J.R. Weidman, A. Cato and L.Y. Sutton: I have financial interest in this product. All other authors have declared no conflicts of interest.

Background: Pancreatic cancer cells and surrounding stroma are known to overexpress SPARC (secreted protein acid rich in cysteine), which is associated with poor clinical outcomes. In a preclinical model, nab-paclitaxel, an albumin-bound nanoparticle form of paclitaxel, together with gemcitabine (G) has been shown to deplete the tumoral stroma and achieves higher intratumor concentrations of both therapeutic agents when administered in combination vs alone. This phase 1/2 study was designed to evaluate the safety and efficacy of nab-paclitaxel + G, correlated with SPARC and serum CA19-9 levels.

Methods: nab-Paclitaxel (100-150 mg/m2) + G (1000 mg/m2) were given on days 1, 8, and 15 of a 28-day cycle to previously untreated patients (pts) with metastatic pancreatic adenocarcinoma. SPARC expression signature in the tumor was evaluated for 7 components microscopically to discriminate pts with low and high risk of death. Results: Of the 67 treated pts, the most common grade 3/4 treatment-emergent adverse event (TEAE) that occurred in >20% of pts was neutropenia and fatigue. Thirty-nine (58%) pts and 17 (25%) pts had a TEAE grade 3/4 event, respectively. Grade 3 neutropenia was observed in 9 (13.5) pts. By RECIST criteria, of the 67 pts evaluable to date, 3 (4%) had complete response, 28 (42%) had partial response, and 12 (18%) had stable disease 216 weeks. The median survival was 10.3 months (all arms), with 12.2 months in the 125 mg/m2 arm. Survival and response were collated with SPARC signature (13.6 vs 8.1 median months in the low vs high risk, P = 0.02). All evaluable pts had an >20% decrease in CA19-9 levels, which is historically associated with improved survival. Conclusions: The combination of nab-paclitaxel + G, in particular the 125 mg/m2 arm, was well tolerated and produced substantial efficacy in patients with pancreatic cancer. Additionally, survival was correlated with SPARC signature in these pts. Based on these results, a phase 3 clinical trial is currently enrolling patients.

Disclosure: N. Desai: I am an employee of Abraxis BioScience and hold patent for the investigational drug. J. Iglesias: I am an employee of Abraxis BioScience. All other authors have declared no conflicts of interest.

Background: Gemcitabine-based chemotherapy (GBC) is a standard first-line treatment in advanced pancreatic cancer. In gemcitabine-pretreated pancreatic cancer, salvage chemotherapy has not yet been established and the prognostic factors have not been widely known. The purpose of this study was to evaluate the efficacy and safety of IFAM in gemcitabine-pretreated pancreatic cancer and to reveal the prognostic factors. Methods: Eligibility included: 1) age 18-75, 2) histologically confirmed pancreatic cancer 3) relapse within 6 months after adjuvant GBC or previously treated with palliative GBC, 4) ECOG PS 0-2, 5) adequate organ function. IFAM consisted of 5-FU 800 mg/m2 over 10 hour on days 1-5, doxorubicin 30 mg/m2 on day 1 and mitomycin-C 8 mg/m2 on day 1, every 4 weeks. Results: Between Feb 2003 and Aug 2009, 60 patients (pts) were enrolled. The median age was 57.4 yrs (range: 35.4-74.1 yrs), and there were 43 men (71.7%). 40 pts (66.7%) had ECOG PS 0-1 and 20 pts (33.3%) had PS 2. The median follow-up duration was 5.2 months (range: 0.6-61.5). Median cycles of IFAM were 2 (range: 1-10). The relative dose intensity of each drug was 87.6% in 5-FU, 87.7% in doxorubicin and 87.7% in mitomycin-C. Best responses to IFAM were PR in 6 (10.0%) pts and SD in 8 (13.3%), that is response rate was 10.0% (95% CI: 2.4-17.6) and disease control rate was 23.3% (95% CI: 12.6-34.0). The median TTP and OS were 2.4 (95% CI: 2.0-2.8) months and 5.9 (95%
GEMCITABINE (G) FIXED RATE DOSE INFUSION (FDR) PLUS EPLORONIB (E) IN PATIENTS WITH ADVANCED PANCREATIC CANCER (APC)

A. Muthu1, E. Azkona1, E. Izquieta2, M. Martinez2, G. Lopez-Aviano2, R. Fernandez1, A. Ruiz-Ts Lobera1, I. Rubio1, R. Casas3, J.M. Mane1
1Medical Oncology, Hospital de Cruces, Barakaldo/SPAIN, 2Hospital de Cruces, Barakaldo/SPAIN

Background: G (50-minute infusion) plus E improves survival in patients with APC compared with G alone. In a recent phase III trial, G-FDR showed a trend to better OS compared with standard G (6.2 vs 4.9 months, HR 0.83, p=0.04), although the study was underpowered to detect a great difference in OS. In our previous experience with G-FDR, we decided to evaluate the combination of G-FDR plus E, after E approval for APC.

Patients and methods: Patients with previously untreated pathologically confirmed APC, locally advanced (LAPC) or metastatic (MPC), and ECOG PS 0 to 2 were included. G 1500 mg/m² was given by 50-min infusion (10 mg/m²/min) on days 1, 8 and 15 every 28 days combined with E 100 mg/day orally. Treatment modifications for G-FDR were planned according to previous Tempero’s phase II trial, and as described in prescribing information for E.

Results: 62 pts were included (36M/26F, with a median age of 63 y-o (range 37-78)). EGC2 PS 0/1/2: 19/40/3. LAPC/MPC: 16/46. All except one had measurable disease. ORR was 13% (95% 4.7-21.5), and there were 34 (55%) SD. Mean relative dose intensity for G was 0.76 and 0.90 for E. Main hematologic toxicities 3/4 per pt: anemia 12/0, thrombocytopenia 7/4, neutropenia 18/0. Acneiform rash 1/23 occurred in 16/16/3 pts. Other relevant adverse events were (grade 2/3/4): diarrhea 18/3/0, mucositis 5/1/0, infection 9/8/1, thrombosis 1/4/1 and vomiting 6/4/0. There were 3 treatment-related deaths (septic shock, cholangitis and bilateral pulmonary embolism). Ten pts (all LAPC) received RT after 6 cycles, all with concomitant Capectarbine 825 mg/m² bid. In 4 pts surgery was performed: 2 R0, 1 R1 and 1 R2. Median PFS was 4.9 months (95% CI: 3.6-7). 7.9 m for LAPC and 2.5 m for MPC (p=0.004). Median OS was 10 months (95% CI: 7.1-12.9), 17.5 m for LAPC and 7.5 m for MPC (p=0.019). OS was significantly shorter in males (p=0.01) and in pts (p=0.004). Median OS was 10 months (95% CI: 7.1-12.9), 17.5 m for LAPC and 7 m for MPC (p=0.019). OS was significantly shorter in males (p=0.01) and in pts (p=0.004). There was a trend to better OS in pts who developed skin rash grade 2 (p=0.078).

Conclusions: In this non comparative study, G-FDR plus E is a feasible regimen in APC with an acceptable toxicity and notable activity. G-FDR seems to increase haematological toxicity compared with standard infusion.

A PROGNOSTIC MODEL TO IDENTIFY PATIENTS WITH ADVANCED PANCREAS ADENOCARCINOMA WHO COULD BENEFIT FROM SECOND LINE CHEMOTHERAPY

1Division of Hematology-Oncology, 1Department of Medicine, Korea University Aram Hospital, Korea University College of Medicine, Seoul/SOUTH KOREA, 2Internal Medicine, Korea University Hospital, Seoul/SOUTH KOREA, 3Korea University Aram Hospital, Korea University College of Medicine, Seoul/SOUTH KOREA, 4Medical Oncology, Korea University Guro Hospital, Seoul/SOUTH KOREA

Background: The role of salvage chemotherapy after first line therapy in advanced pancreatic cancer has not yet been established. We intended to predict prognostic factors for long-term survival of advanced pancreatic adenocarcinoma patients with second-line chemotherapy and to devise a prognostic model on clinical parameters. Patients and methods: We analyzed 90 patients who had received second line chemotherapy after the failure of first line therapy in recurrent or metastatic pancreatic adenocarcinoma between August 2003 and December 2008.

Results: The median age at the time of second line chemotherapy was 61-9 years (range 39-84), and the median Karnofsky performance status was 1 (0-2). Median progression free survival (PFS) and overall survival (OS) for second line chemotherapy were 2.1 and 4.5 months, respectively, with an overall response rate of 10%. In multivariate analysis, ECOG PS of 2 or more, non-responder for first line chemotherapy and albumin level of <3.5g/dl were independent prognostic factors for decreased OS for all 90 patients. OS was estimated based on the number of adverse prognostic factors: zero or one (good prognostic group), two (intermediate group), or three (poor prognostic group). The median OSs for good (n=50), intermediate (n=24), and poor (n=16) were 5.5, 3.3, and 2.1 months, respectively (p=0.001).

Conclusion: Our result suggests that second line chemotherapy may be beneficial for overall survival in patients with ECOG PS 0-1, albumin level ≥3.5g/dl and good response for first line chemotherapy.

Disclosure: All authors have declared no conflicts of interest.

Pancreatic cancer is a particularly challenging malignancy given its usually advanced stage at diagnosis and its rather limited response to treatments. Although gemcitabine is the backbone of routine therapy in advanced disease, novel drugs are urgently needed for improving the treatment of this cancer. Overexpression and activation of tyrosine kinase receptors are common features in pancreatic cancer. The aim of this study has been to evaluate if combined inhibition of EGFR, Her-2 and IGF-IR may overcome the resistances observed in monotherapy strategies. Moreover, molecular changes involved in resistance observed in monotherapy may be exploited for repositioning of drugs. Resistance to gemcitabine (G) and erlotinib (E) has been associated with activation of the PI3K/Akt and MEK/ERK pathways, respectively. In this study, we have investigated if combined inhibition of EGFR, Her-2 and IGF-IR may overcome the resistances observed in monotherapy strategies. Moreover, molecular changes involved in resistance observed in monotherapy may be exploited for repositioning of drugs.
arrest at G1 and apoptotic cell death. The analysis by Western Blot of proteins involved in Erk and IGF-IR signaling pathways demonstrated that although each drug was able to reduce the activity of IGFRI, the combination treatment caused a marked reduction of the activated status of all three effectors. In conclusion, the combined inhibition of Erk and IGF-IR may solve the resistance due to bidirectional transactivation of these receptors, representing a very promising therapy against an important percentage of human pancreatic tumors.

Disclosure: All authors have declared no conflicts of interest.

**T71P**

**POTENTIATION OF GEMCITABINE EFFECTS WITH A CETUXIMAB AND TRASTUZUMAB COMBINATION IN A NOVEL HUMAN PANCREATIC ORTHOTOPIC MODEL**


1Biochemistry and Molecular Biology, Institute of Biomedicine, Barcelona SPAIN, 2Department of Medical Oncology, Hospital Clinic, Barcelona SPAIN

Introduction: Treatment of pancreatic cancer remains challenging and mostly palliative. Cetuximab and erlotinib has shown modest benefit compared with gemcitabine alone. The efficacy of anti-EGR therapies has been possibly hampered by the absence of biomarker selected strategies. Activation of compensatory pathways, such as Her-2 or IGF-IR signaling, should be considered.

Methods: Fourteen xenografts only one shows moderate to high levels of both EGFR and Her-2 and very low IGF-1R activity. The other models harbor null or very low levels of either ErbB or IGF-IR signaling, should be considered. Consequently, it cannot be fully excluded that the results of the present study might not be representative for all pancreatic tumors.

Results: Combination of cetuximab and trastuzumab with gemcitabine potentiated intrapancreatically in nude mice and expanded to develop cohorts of tumor bearing EGFR and Her-2 and very low IGF-1R activity. The other models harbor null or very low levels of either ErbB or IGF-IR signaling, should be considered. The other models harbor null or very low levels of either ErbB or IGF-IR signaling, should be considered.

Conclusions: Cetuximab and trastuzumab with gemcitabine potentiated tumor growth inhibition (p<0.05, triple treatment vs double treatments) in xenografts of pancreatic cancer cells. Until further randomized studies, anti-EGR therapies have been probably hampered by the absence of biomarker selected strategies. Therefore, the present study represents a promising strategy in pancreatic tumors with activated EGFR and Her-2 but without activation of IGF-1R pathway.

Disclosure: All authors have declared no conflicts of interest.

**Efficacy and safety of Sorafenib (Sor) in patients (pts) with advanced hepatocellular carcinoma (HCC): subgroup analyses of the Sharp and Asia-pacific (AP) trials by baseline (BL) Transaminase (ALT)/Alpha-FetoProtein (AFP) and Bilirubin (BIL) levels**

J. Raoul1, A. Cheng2, S. Yu3, T. Yang1, A. Nadef4, F. Fang3, G. Lentini3, J. Zou4, J.M. Llovet3, J. Brux1

1Department of Oncologie Medicale, Centre Eugène Marquis, Renner, FRANCE, 2Hepatologie/oncologie, National Taiwan University Hospital, Taipei, TAIWAN, 3Tongji Medical College, Huazhong University of Science and Technology, Wuhan/CHINA, 4Chang Gung Memorial Hospital, Linkou/TAIWAN, 5Bayer HealthCare Pharmaceuticals, Montville/UNITED STATES OF AMERICA, 6GI Oncology, Bayer Vital GmbH, Leverkusen/GERMANY, 7Medical Affairs Asia, Bayer Schering Pharma, Shanghai/CHINA, 8Mount Sinai School of Medicine, Mount Sinai Liver Cancer Program, New York/UNITED STATES OF AMERICA, 9Liver Unit, Institut De Malaties Digestives, University of Barcelona, Barcelona SPAIN

Introduction: We examined the effect of Sor on hepatic function as indicated by Bil levels, and performed subset analyses of the Sharp and AP trials according to BL levels of ALT/AST, AFP, and Bil.

Methods: Eligibility criteria were similar for the 2 trials. Pts had advanced HCC. Child-Pugh class A, ECOG PS 0–2, and no prior systemic therapy for HCC. Pts were randomized to Sor 400 mg bid or placebo (Pla) at a 1:1 (SHARP) or 2:1 (AP) ratio. Endpoints included overall survival (OS), disease-control rate (DCR) defined as complete/partial response or stable disease by RECIST maintained for 24+ days from first demonstration of response), time to progression (TTP), and safety. Pts were grouped by BL levels of ALT/AST, AFP, and Bil. Median time at Bil and day 1 of each cycle.

Results: OS and DCR are shown below. No notable differences in safety profiles were observed between Pts with normal vs elevated AFP or Bil levels or not significantly elevated vs mildly/moderately elevated ALT/AST levels. Median BL levels of Bil in the Sor and Pla groups were similar across cohorts for each study. No consistent differences in Bil levels were observed between the Sor and Pla groups by cycle in either trial. Median increases in Bil at last cycle were similar in the Sor and Pla groups for both studies.

Conclusions: Pts with elevated Bil levels of AFP or Bil or mildly/moderately elevated ALT/AST had shorter OS than those with normal AFP or Bil levels or not significantly elevated levels of ALT/AST, regardless of treatment. However, the results of our subset analyses suggest that Sor is a safe and effective treatment for HCC, irrespective of ALT/AST, AFP, or Bil levels, and that hepatic function (Bil levels) is not affected by Sor.

Disclosure: The authors have declared no conflicts of interest.

**751P**

**QUALITY OF LIFE ASSESSMENT WITH COMBINED EORTC QLQ-C30 AND EORTC-HCC18 AS A PROGNOSTIC FACTOR FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA: A PROSPECTIVE STUDY**

L. Li1, S.L. Chan1, F. Mo1, J. Koh1, E.P. Hui1, B. Ma1, T.S.K. Mok2, A.T.C. Chan3, W. Yeo1

1Department of Clinical Oncology, The Chinese University of Hong Kong, Shatin/HONG KONG, 2Department of Clinical Oncology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin/HONG KONG, 3Oncology, The Chinese University of Hong Kong, Shatin/HONG KONG

Background: For patients (pts) with hepatocellular carcinoma (HCC), patient-reported quality of life (QoL), as measured by EORTC QLQ-C30 (C30), was an independent prognostic factor (Yeo W et al. Ann Oncol. 2006). EORTC QLQ-HCC18 (HCC18) has been derived and suggested to supplement the C-30 in measuring QoL for HCC. We aimed to investigate the significance of the combined assessment with 2 tools in prognostication of overall survival in HCC pts.

Methodology: Pts with newly diagnosed HCC were recruited prospectively and followed (Sor/Pla)Sor Pla Median (mo) HR (95% CI)

<table>
<thead>
<tr>
<th>Population</th>
<th>n</th>
<th>OS (Sor/Pla)</th>
<th>DCR (%) (Sor/Pla)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>299</td>
<td>303</td>
<td>10.7/7.9</td>
</tr>
<tr>
<td>SHARP</td>
<td>150</td>
<td>76</td>
<td>6.5/4.2</td>
</tr>
<tr>
<td>AP</td>
<td>86</td>
<td>26</td>
<td>8.2/8.0</td>
</tr>
<tr>
<td>SHARP</td>
<td>77</td>
<td>78</td>
<td>9.5/8.5</td>
</tr>
<tr>
<td>AP</td>
<td>153</td>
<td>97</td>
<td>7.2/4.7</td>
</tr>
<tr>
<td>SHARP</td>
<td>111</td>
<td>97</td>
<td>12.4/8.5</td>
</tr>
<tr>
<td>AP</td>
<td>116</td>
<td>59</td>
<td>6.1/4.1</td>
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<tr>
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<td>225</td>
<td>226</td>
<td>11.9/9.1</td>
</tr>
<tr>
<td>AP</td>
<td>103</td>
<td>46</td>
<td>7.2/4.3</td>
</tr>
<tr>
<td>SHARP</td>
<td>227</td>
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</tr>
<tr>
<td>AP</td>
<td>135</td>
<td>29</td>
<td>5.2/3.9</td>
</tr>
</tbody>
</table>

ULN=upper limit of normal. *3 Pts in the AP trial had ALT/AST levels >5.0 x ULN, and are not included in this analysis.

Disclosure: J. Raoul: Bayer - advisory boards, lecture fees BMS - advisory boards, lecture fees A. Cheng: received honoraria from Bayer; A. Nadef: employee of Bayer; F. Fang and G. Lentini: a stock owner and an employee of Bayer; J. Zou: an employee of Bayer; J.M. Llovet: Bayer - research support, consultancy agreement BMS - research support, consultancy agreement Johnson and Johnson - research support Exelixis - research support Abbott - consultancy agreement Biocompanents - consultancy agreement. J. Brux: Bayer - consultation fees, research grant Eli Lilly - advisory committees BMS - advisory committees Novartis - advisory committees Bicospanals - advisory committees, research grant Ensi - advisory committees Bracco - speaking and teaching. All other authors have declared no conflicts of interest.

Notes: 28 days from
Annals of Oncology

loss of appetite to be significant prognostic factors, while that on HCC18 showed nutritional status and sexual interest to be significant. Analyses on combined assessment with C30 and HCC18 found only HCC18 items to be significant. Analyses on the 2 tools and other clinical factors identified high AFP (p < 0.001; HR=1.120), bilirubin (p < 0.001; HR= 1.095), advanced CUPI staging (p < 0.001; HR=2.083), curative treatment (p=0.0083; HR=0.236) and worse (Qol score in HCC18 fatigue scale (p=0.0014; HR for 1 point increase=1.124) to be significant.

Conclusions: For pts with HCC, EORTC HCC18 appears to more significant than EORTC-C30 in prognostication. On top of conventional prognostic factors, HCC18 fatigue scale is an independent prognostic factor.

Disclosure: All authors have declared no conflicts of interest.

Preliminary Pharmacokinetics (PK) and Safety Comparison of Child-Pugh A (CPA) vs. Child-Pugh B (CPB) Patients (PTS) Enrolled in a Phase 2 Study in Hepatocellular Carcinoma (HCC)

N. Gupta1, Y. Chiu2, H.C. Toh3, P. Chen4, W. Yong4, M. McKee4, J.L. Ricker6, D.M. Carlson6, R. Pradhan7

1R4PK, Abbott Park/UNITED STATES OF AMERICA, 2Clinical Pharmacology and Pharmacometrics, Abbott Laboratories, Abbott Park/UNITED STATES OF AMERICA, 3National Cancer Center, SINGAPORE, 4National Taiwan University Hospital, Taipei/TAIWAN, 5Division of Transfusion Medicine and Department of Medicine, Chang Gung General Hospital and National Yang Ming School of Medicine, Taipei/TAIWAN, 6Hepatology/oncology, National Taiwan University Hospital, Taipei/TAIWAN, 7Philippine General Hospital, Manila/PHILIPPINES

Background: Linifanib (AR-869) is a novel orally active and selective inhibitor of VEGF and PDGFr families of receptor tyrosine kinases. Pharmacokinetic (PK) data indicates that the time to maximum plasma concentration is approximately 3 hr and the elimination half-life is 1 day. The PK appeared dose-proportional between 0.10 mg/kg and 0.30 mg/kg and time-invariant after repeated dosing from 1W (D) 1 to 15.

Methods: This phase 2 study is being conducted in Singapore, Taiwan, Hong Kong and North America to determine the efficacy and to establish the safety/toxicity profile of linifanib in pts with advanced hepatocellular carcinoma (HCC). On Study Day (D) 1, after administration of morning dose oral linifanib 0.25 mg/kg, PK samples were collected over 48 hours from 14 pts (9 CPA and 5 CPB). Linifanib exposures (Cmax and AUC) were calculated by non-compartmental analysis using WinNonlin Professional V.5.2. One pre-dose blood sample was collected on D1 for determination of plasma protein binding to help calculate free exposures. No dose was given on D2, and pts began evening dosing on D3. Linifanib was dosed once daily for CPA pts and every other day for CPB pts, with no food or beverage 2-hrs before and after linifanib dose in a 21-D cycle.

Results: Based on preliminary data from 9 CPA and 5 CPB pts, there appears to be no difference in total and unbound linifanib exposures (measured as Cmax and AUC). Median Tmax was approximately 3 hours for both CPA and CPB pts. Pts with and without hepatic impairment had similar exposures suggesting that no dose adjustment is needed for hepatic impaired pts. The mean number of days on linifanib was 45.5 (range, 4-429) and 50.5 (range, 11-111) in CPA and CPB pts, respectively. Linifanib-related adverse events (AEs) occurred in all 38 CPA pts (100%) and 6 CPB pts (100%). Linifanib-related serious AEs occurred in 13 of 38 CPA pts (34.2%) and 3 of 6 CPB pts (50%).

Conclusion: The presence of hepatic impairment or its extent in cancer pts (CPA vs. CPB), does not influence Linifanib PK.

Disclosure: N. Gupta, Y. Chiu, M. McKee, J.L. Ricker, D.M. Carlson and R. Pradhan: Full-time employee of Abbott Laboratories. All other authors have declared no conflicts of interest.

Efficacy and Tolerability of Bevacizumab (B) and Erlotinib (E) as First-Line Therapy in Asian Patients (PTS) with Advanced Hepatocellular Carcinoma (HCC): A Phase II Trial


1Dept of Oncology, National Taiwan University Hospital, Taipei/TAIWAN, 2Division of Oncology, Department of Internal Medicine, Asian Medical Center, Taoyuan/SOUTH KOREA, 3Hepatology/Oncology, Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taoyuan/TAIWAN, 4National Cheng Kung University Hospital, Tainan/TAIWAN, 5Medical Oncology, Philippines General Hospital, Manila/PHILIPPINES, 6Division of Transfusion Medicine and Department of Medicine, Taipei Veterans General Hospital and National Yang Ming School of Medicine, Taipei/TAIWAN, 7Oncology, Roche Australia, Dee Why/AUSTRALIA, 8Hepatology/oncology, National Taiwan University Hospital, Taipei/TAIWAN

Background: Asian pts with advanced HCC have a poor prognosis and a median OS of 2–4 months with best supportive care (Hsu et al., 2010). Although sorafenib has demonstrated improved median OS of 6.5 months (Cheng et al., 2009), there is still a substantial unmet medical need. Dual inhibition of VEGF and EGFR with B+H is an attractive strategy in HCC. Encouraging efficacy was reported with B+H in a Western population (Thomas et al., 2009). This trial was initiated to investigate the safety and efficacy of B+H in Asian pts.

Methods: Pts with advanced HCC received B 5mg/kg q2w i.v. and E 150mg/day p.o. as first-line therapy. Screening esophagogastroduodenoscopy (EGD) was used to exclude pts with high risk of variceal bleeding. The primary endpoint was PFS at 16 weeks, with response assessed by RECIST. Other endpoints were OS, overall response rate (ORR), disease control rate (DCR) and safety. Pre-treatment tissue samples were collected.

Results: Fifty-one pts were enrolled. Baseline characteristics were as follows: median age 58 years (range 26–84); male/female: 44/7; ECOG performance status 0/1/2: 30/0/16; Child-Pugh A/B: 30/1; BCLC stage C: 44 (88%); hepatitis B/C:B/C+: 50/1; Child-Pugh A/B: 50/1; BCLC stage C: 42/3/2; grade 1/2 varices: 16 (none with red sign). Forty-three pts (84%) had extrahepatic metastasis and/or major vessel invasion. Nineteen (37%) had prior resection; 25 (49%) received prior trans-arterial chemoembolisation (TACE)/TAE for HCC. Treatment-related toxicities (TRT) were mostly grade 1/2. Grade 3 TRTs in >1 patient were: rash (n=3), diarrhea (n=2), increased transaminases (n=3), hyperbilirubinaemia (n=3), proteinuria (n=2) and GI bleeding (n=2). Only one grade 4 TRT was reported: gastric variceal bleeding, which resolved. PFS at 16 weeks was 29.9 months (95% CI 18.4–48.9) and median OS was 10.7 months (95% CI 7.4–NR). ORR was 6% and DCR was 53%. Among 31 pts, 26 received subsequent systemic therapy: either TKI (11 pts) or chemotherapy (15 pts). Results of biomarker analyses will be reported.

Conclusion: The B+H combination is well tolerated and showed encouraging efficacy in this Asian population.

Disclosure: Y. Kang: I have taken part in advisory boards for Roche, Bayer, Pfizer. T. Chiu: Advisory boards for: GSK, JTP and CLL, Novartis Taiwan-CML Corporate sponsored research: Pfizer Taiwan and GSK. K. Lin: Full time employee of Roche Australia. All other authors have declared no conflicts of interest.

Management and Cancer Outcomes of Secondary Malignancies Following Liver Transplantation

H.L. Martin1, B. Koczwara2

1Medical Oncology, Flinders Medical Centre, Bedford Park/SA/ AUSTRALIA, 2Medical Oncology, Flinders Medical Centre, Adelaide/AUSTRALIA

Background: Transplant recipients are at high risk for development of malignancy. Data from renal transplantation recipients shows almost two-fold higher rates of cancer among renal survivors developing cancer. Malignancies in the post transplant population prove a significant management challenge for oncologists due to the difficulty of balancing preservation of the transplanted organ, the toxic side effect profile of the immunosuppressant agents used, and the possible interactions between chemotherapeutic agents and the immunosuppressants. To date there are no guidelines for care of solid organ transplant recipients. We have reviewed the management and cancer outcomes of patients who develop malignancy post liver transplantation in order to identify key management challenges in this setting.

Methods: This was a single centre retrospective audit. The liver transplant unit database was used to identify patients who had developed malignancy. The database was also cross checked against the Cancer Registry to ensure all patients were identified. The medical records and investigation results of patients identified as having developed secondary malignancies were reviewed. Descriptive analysis of this information was then performed.

Results: Post transplantation malignancies were common. Of the 200 transplant recipients followed through from 1992 to May 2010, 53 patients were identified. The most frequent cancers were squamous cell and basal cell carcinoma of the skin. Other malignancies included hepatocellular carcinoma, prostate cancer, adenocarcinoma of the bowel and lymphoma. There was variation in the management of the immunosuppressive regimen following diagnosis of malignancy. There was a significant rate of chemotherapy related toxicity amongst the group who received chemotherapy. Detailed analysis will be included at the time of presentation.

Conclusion: post transplantation malignancies have been shown to present a significant challenge in terms of management. Further prospective studies are required to enable guidelines development for management of these malignancies.

Disclosure: All authors have declared no conflicts of interest.

Abstracts
Conclusion: Smoking is related to increased risk of all major types of GI cancer except colorectal. Alcohol drinking has only a weak relation to colorectal cancer and none to cancer of the stomach or pancreas.

Disclosure: All authors have declared no conflicts of interest.

757 CAPECITABINE AND CISPLATIN PLUS CONCOMITANT RADIATION THERAPY IN PATIENTS WITH LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS (LA-SCCE)

1Servico de Oncologia Clinica, Hospital de Clinicas de Porto Alegre, Porto Alegre/BRASIL; 2Hospital de Clinicas de Porto Alegre, Porto Alegre/BRASIL

Background: Lee and cols. (1 Korean Med Sci 2009) described a high complete response (CR) rate and a favorable overall survival (OS) in the cisplatin-free chemoradiotherapy with capecitabine and cisplatin in a pilot study including 18 patients with LA-SCCE. The capcitabine/cisplatin doublet plus concomitant radiationtherapy is a non-inferior alternative for the treatment of LA-SCCE. Here, we describe our institutional experience with this combination.

Methods: Twenty-three consecutive patients with unsatisfactory LA-SCCE were accrued between July 2008-July 2009. They received weekly cisplatin at the dose of 30 mg/m², starting on day 1, for weeks 1-5, and orally capecitabine, 1600 mg/m², on days 1-5 for weeks 1-5, plus radiation therapy (54Gy/2Gy/day, 5 days/week) on weeks 1-5. Two additional courses of cisplatin 75 mg/m²/d1 and capecitabine 2000 mg/m²/d1-d4 were delivered. Study endpoints were clinical response (including biopsy) and endoscopic evaluation and safety profile.

Results: The mean age was 56 years, 82.6% of cases with stage III disease and 95% had PS 0-1 (ECOG). All, except 4 patients, completed the planned treatment, with therapy being discontinued due to toxicity in 2 cases. Two patients were lost from follow-up. Sixteen patients (69.6%) were evaluable for response. CR, PR/stable disease and progressive disease were documented in 75%, 6.3% and 18.2% of cases, respectively. Median OS for CR and CR patients were 7.5 and 17 months, respectively (p=0.01). All patients were evaluable for toxicity, with severe (grade 3-4) nausea/vomiting/diarrhea, asthenia and neuropenia being observed in 17.4%, 13% and 8.7%, respectively. One treatment related death was documented (4.4%).

Conclusions: Our results confirm previous observations that concurrent chemoradiotherapy with capcitabine and cisplatin is a well-tolerated and highly active regiments for the treatment of patients with LA-SCCE. Prospective randomized trials are needed to evaluate the role of capcitabine compared to 5-FU in the above combination.

Disclosure: J. Broilo: Education grants: Roche. R. Weschenfelder: Research grants: Roche Speaker: Roche Education grants: Roche. All other authors have declared no conflicts of interest.

758 PHASE II STUDY OF DOXETAXEL AND 5-FLUOROURACIL WITH CONCURRENT RADIOTHERAPY IN PATIENTS WITH ADVANCED ESOPHAGEAL CANCER

J. Hihara, Y. Hamai, M. Eri, Y. Aoki, Y. Miyata, M. Okada
Surgical Oncology, Research Institute for Radiation Biology and Medicine, Hiroshima University, Hiroshima/JAPAN

Background: Although cisplatin plus 5-FU-based chemoradiotherapy is the most frequently used program in esophageal cancer treatment, it has limited efficacy. We have performed phase I study, combining weekly administration of docetaxel and continuous infusion of 5-FU with concomitant radiotherapy for locally advanced esophageal cancer (Anticancer Res 27:2997,2007). We subsequently conducted phase II study according to the recommended dose (7.5mg/m²) of docetaxel in phase I study.

Methods: Patients (Pts) with locally advanced esophageal cancer who have adequate organ function were eligible. Pts with distant lesions extending beyond the radiation field were not eligible for this phase II study. During chemoradiotherapy, docetaxel were given at a dose of 7.5mg/m² at D1, D8, D22, D29, D45. D5. 5-FU 250mg/m²/day was administered by continuous infusion for 24h on the same day of radiation (3 days/week). A total dose of 60 to 66 Gy was delivered in 2 Gy per fraction.

Results: 26 pts (7 pts in phase I and 19 in phase II) were enrolled and all pts were eligible. In phase II study, the median age was 63 (range 44-78); male/female: 15/4; PS 0/1: 16/3; histology: SCC; 19 (100%); tumor location cervical/thoracic: 5/14: UICC (6th ed.):stage III(1)/IVa(1)/b(1)/: 2306.22: Complete response was achieved in 6 pts (31.6%), partial response in 11 (57.9%), and 2 pts had progressive disease (10.5%). Over the CTC grade 2 hematological toxicities were not seen. The most common non-hematologic toxicity was esophagitis. Grade 3 or 4 of esophagitis has been developed in 5 pts (26.3%). 11 pts experienced recurrent disease, MST was 18 months and 3-year overall survival was 42.1%.

Conclusions: Concurrent chemoradiotherapy with docetaxel and 5-FU was well tolerated and promising for pts with locally advanced esophageal cancer.

Disclosure: All authors have declared no conflicts of interest.
Palliative High Dose Rate Brachytherapy is an effective and well tolerated treatment for the dysphagia of recurrent oesophageal cancer. Brachytherapy improves quality of life and could potentially have an impact on survival. More studies need to be performed to identify biomarkers of response to brachytherapy that could lead to better patient selection.

Disclosure: All authors have declared no conflicts of interest.

References


Disclosure: All authors have declared no conflicts of interest.

Abbreviations
CR: Complete response
PR: Partial response
SD: Stable disease
PD: Progressive disease
CR+PR: Complete/partial response
SD/CR: Stable disease to complete response
HR: Hazard ratio
CI: Confidence interval
BMI: Body mass index
PS: Performance status
N: Number
M: Median
OS: Overall survival
DFS: Disease free survival
PFS: Progression free survival
RR: Risk ratio
ET: Elective neck dissection
CRT: Chemoradiotherapy
SDC: Symptomatic dysphagia control
DCRT: Definitive chemoradiotherapy
NE: Not estimable
DCS: Debulking surgery
T: Tumour
N: Node
M: Metastasis

Purpose: We performed multicenter retrospective study to evaluate the activity and the safety of a docetaxel as salvage chemotherapy in advanced gastric cancer patients who had undergone oxaliplatin (FOLFOX) and irinotecan (FOLFIRI) based sequential chemotherapy regimens.

Methods: Thirty-eight patients with advanced gastric cancer previously treated were eligible for this study. Patients received docetaxel 30mg/m² iv day on day 1, 8 or docetaxel 60mg/m² iv day on day 1 every 3 weeks until disease progression or death. The median progression-free survival (PFS) was 1.8 months (95% CI: 1.3-2.3 months). The median overall survival (OS) was 3.1 months (95% CI: 2.3-3.9 months). Good performance status (ECOG 0-1) in patients was predictive of longer PFS and OS. Bone metastasis with patients were predictive of shorter OS. Grade 3 or 4 hematologic toxicities included neutropenia in thirteen patients (38%), febrile neutropenia in four patients (11.7%) and thrombocytopenia in one patient (2.9%). Other grade 3 or 4 toxicities included neuropathy (8.8%) and pneumonitis in two patients (5.9%). There were three treatment-related deaths (8.8%) caused by infection associated with neutropenia.

Conclusion: Salvage docetaxel chemotherapy in AGC patients failed in oxaliplatin and irinotecan based treatment is not recommended routinely. However, selected patients with good performance status may have derived some survival benefits from salvage chemotherapy.

Disclosure: All authors have declared no conflicts of interest.

A PHASE II STUDY WITH CAPECITABINE AND CISPLATIN AS FIRST-LINE THERAPY IN ADVANCED GASTRIC CANCER

P.J. Forseca1, J.M. Vélez2, M. Frunza1, J.P. Berros2, M. Fernandez De Samnnaře2, C. Muru2, M. Izquierdo1, P. Parodi1, E. Gutierrez1, A. Jacave1

1Oncology Department, Hospital Central de Asturias, Oviedo/SPAIN, 2Medical Oncology, Hospital Universitario Central de Asturias, Oviedo/SPAIN

Background: Nowadays, randomized phase III studies’ results show marginal differences concerning the survival rate in first-line therapy in advanced gastric cancer (AGC) and do not strongly support the use of a specific protocol as standard treatment. Objectives: evaluate the efficiency (global response rate, time to progression, overall survival) and safety of the low-doses of XC. (Capecitabine + Cisplatin).

Patients and methods: 42 patients (pts) with histopathologically confirmed metastatic AGC who had not underwent previously chemotherapy, more than 18 years old and with Karnovsky (PSk) 0-4% treated with Capecitabine (XC) 850mg/m² bid. for 14 days and Cisplatin (C) 70 mg/m² iv day 1 every 3 weeks until disease progression. The recommended low-doses for this phase II study were obtained in our previous phase I trial.

Results: Between June 2005 and June 2009, 42 pts (32 male/10 female) were treated with the protocol. The median age was 62 years (range, 39-79) and 14 pts (33%) had more than 65. Median KPS: 70%. Number of metastatic sites: 1, 21 pts, 2, 15 pts and 3 or more, 6 pts. Involved metastatic organs: nodes (n=25), liver (n=19), peritoneum (n=15), lung (n=8), others (n). The median of the cycles of chemotherapy received was 6 (range, 1-12). Efficiency: 13% completed response (2.8%) and 14 pts with partial response (40%), ORR of 42.86% (95% CI: 25.45-62.59). Median time to progression was 5 months (95% CI: 4.7-6 months) and overall survival rate was 11 months (95% CI: 10-14 months). Tolerance: 2 pts with grade 4 toxicity. Grade 2-4 toxicity: vomiting 62%, neutropenia 40%, hand-foot syndrome 36%, mucositis 24%, alopecia 22%, anemia 19% and 12% respectively, diarrhea 7% and nephrotoxicity 6%. 16 pts (38%) underwent surgery for primary tumour, 27 pts (65%) received second-line chemotherapy (docetaxel) and 7 pts (17%) received a third-line treatment (irinotecan + bevacizumab).

Conclusions: The XC doses used in the study showed not only an efficiency and a survival rate comparable with the high ones (Kang YK, Ann Oncol 2009;20(4):666-73) but also minor and more manageable toxicity fact that could make them a better option as first-line treatment in AGC if the results are confirmed by phase III studies.

Disclosure: All authors have declared no conflicts of interest.
Conclusion: Capecitabine is tolerable when given alone or combined with other chemotherapy or radiation. This tolerability ensured good compliance to treatment. Capecitabine compares favorably with FU for advanced gastric cancer.

Disclosure: All authors have declared no conflicts of interest.

FEASIBILITY OF SURGERY FOLLOWED BY CHEMORADIOThERAPY IN GASTRIC CANCER. PHASE II TRIAL

1Department of Oncology, Ahsania Mission Cancer Hospital, Dhaka/ BANGLADESH, 2OncoLOGY, Ahsania Mission Cancer Hospital, Dhaka/ BANGLADESH, 3Oncology, National Institute of Cancer Research and Hospital, Dhaka/BANGLADESH

Background: In Bangladesh usually patients report to oncologists in advanced stages. In case of gastric cancer the fact is also almost regular phenomenon. Patients general conditions and performance status usually not in favour of conventional chemotherapy with cisplatin and taxane. So, we had conducted a phase II study to evaluate the efficacy and safety of biweekly oxaliplatin in combination with continuous infusion 5-fluorouracil and leucovorin (modified FOLOFOX regimen) in Bangladesh elderly patients with advanced gastric cancer (AGC).

Methods: Thirty-five eligible patients older than 65 years with previously untreated AGC and oxaliplatin 85 mg/m2 intravenously over a 2 h period on day 1, together with leucovorin 400 mg/m2 over 2 h, followed by a 46-h infusion of 5-fluorouracil 2600 mg/m2 every 2 weeks. All patients were evaluable for efficacy and toxicity. A median of six cycles (range 3-12) was administered. It was a multi-centic prospective non-randomized study. Performance status of the patient was:

Results: The overall response rate was 48.6% (95% confidence interval (CI): 31-61%) with two complete responses, 16 partial responses, 9 stable diseases, and 8 progressions. Median time to progression was 8.7 months (95% CI: 4.6-7.8) and median overall survival was 10.2 months (95% CI: 8.9-11.8). Toxicity was fairly mild. Grade 3 toxicities included neutropenia (9.7%), nausea (5.3%), vomiting (3.3%), diarrhea (3.2%); and grade 4 toxicities occurred in none of the patients. Grades 1-2 peripheral neuropathy was reported in 41.5% of patients.

Conclusions: The modified FOLOFOX regimen is active, well tolerated as first-line chemotherapy for elderly Bangladeshi patients aged above 65 years with AGC.

Disclosure: All authors have declared no conflicts of interest.

EFFICACY AND NECESSITY OF NASOJEJUNAL TUBE AFTER GASTRECTOMY

S. Noorshafiee1, A. Tavassoli2
1Digestive Oncology Unit, CHU Charles Nicolle InsermU614 University of Rouen, Rouen/France, 2Oncology, La Croix Rousse hospital, Lyon/France

Background: In many centers, nasojejunal tube (NJT) is routinely used for gastrointestinal drainage after total gastrectomy. It is supposed that it would protect anastomosis, but since the stomach should be completely removed, today its efficacy is under question. On the other hand, the tube leads to patients discomfort and aspiration disorders or esophagitis ulceration. The aim of this study is to evaluate the efficacy and necessity of nasojejunal tube after gastrectomy.

Methods: In this interventional study, 50 patients who underwent gastrectomy due to gastric cancer in Ghaem and Omid hospitals related to Mashhad University of Medical Sciences from 2001 to 2008 were enrolled. The patients were randomly divided into two groups of with NJT (25 cases) and without NJT (25 cases). The rate of complications, infective or non-infective, hospitalization duration and the time of beginning diet were evaluated.

Results: Two groups were similar in age, sex, extend of involvement, bleeding volume and length of removed esophagus. There was no significant difference between two groups in the view of first gas passing, beginning of diet, and hospitalization duration. But incidence of sore throat, nasal discomfort, speech disorders, and patients’ unsatisfactory were higher in with NJT group.

Conclusion: It seems that patients without NJT were more comfortable and satisfactory after total gastrectomy. So, there is no need for insertion of NJT after gastrectomy.

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GASTRIC CANCER (GC) ADJUVANT (A) CHEMOTHERAPY (CT): A LITERATURE BASED META-ANALYSIS (MA)

L. Palmer1, D. Matrangos2, M. Vaglica3, A. Marchese4, M. Frazetta5, G. Vestri6
1 Dipartimento di Discipline Chirurgiche e Oncologiche, Universita` di Palermo - Cattedra di Oncologia Medica, PALERMO/ITALY, 2Dipartimento di Biopatologia E Biotecnologie Mediche e Forensi, Universita` di Palermo, PALERMO/ITALY, 3Dipartimento di Discipline Chirurgiche e Oncologiche, Universita` di Palermo, PALERMO/ITALY

The use of ACT in GC is controversial. We performed a MA of the randomized phase III trials concerning this issue. An electronic (MEDLINE, Cochrane) and manual (ASCO and ESMO proceedings, references of selected articles, published reviews) search has been performed. We retrieved the available data from papers published since 1990, aimed to evaluate the effect of ACT after surgery in terms of 5 yr SR and disease free survival rate (DFSR) (HR, 95% Confidence Interval, CI). To avoid potential biases and possibly select the most effective combination, subgroup analysis (SA) for country (EU, USA, Asia), decade of publication (1990-2009, 2000-2009), regimen (anthracycline vs non-anthracycline; oral vs CT), proportion of pts with T3 (570% vs >70%), with a lymph-nodes (LN) resection level >70% (50% vs >50%), with LN+ (570% vs >70%) have been done. A random effects model was used.

We included 18425 studies (4632 pts, 2374 in the investigational, 2392 in the control arm). The administration of ACT resulted in a significant improvement of both 5 yr SR (HR 0.77, 95% CI 0.71-0.85, p<0.005) and DFSR (HR 0.29, 95% CI 0.40 – 0.18). Since the HR, though statistically significant, provides only an estimate of the advantage; the risk difference (RD) for 5 yr SR and DFSR has been evaluated showing ACT is significantly risk-reducing (SR RD -0.07, 95% CI -0.09 – 0.04, p<0.05; DFSR RD -0.08, 95% CI -0.11 – 0.04, p < 0.05).

In the SA a statistically significant HR was confirmed favouring ACT regardless country (Western 0.81 95% CI 0.73 – 0.80, Asia 0.66 95% CI 0.54 – 0.80, p<0.05), decade of publication (1999-1999 0.76 95% CI 0.66 – 0.88, 2000-2009 0.78 95% CI 0.69 – 0.89, p<0.05), drugs administered (anthracycline 0.85 95% CI 0.76 – 0.95, non-anthracycline 0.64 95% CI 0.54 – 0.76; p<0.05), regimen administration (3B vs 2B 0.83 95% CI 0.79 – 0.82, oral 0.85 95% CI 0.84 – 0.87, p<0.05), proportion of pts with T3 (70% vs >70% 0.76 95% CI 0.66 – 0.88, >70% 0.78 95% CI 0.68 – 0.90; p<0.05), LN resection level >70% (50% vs 0.83 95% CI 0.71 – 0.97, >50% 0.74 95% CI 0.65 – 0.85; p<0.05), LN+ (570% vs >70% 0.74 95% CI 0.63 – 0.86, >70% 0.79 95% CI 0.70 – 0.89).

ACT can improve survival for pts radically operated for GC: oral administration of non-anthracycline containing combinations seem to have a superior activity.

Disclosure: All authors have declared no conflicts of interest.

Annals of Oncology
Neutropenia as a Prognostic Factor in Advanced Gastric Cancer Patients Undergoing Second-Line Chemotherapy with Weekly Paclitaxel


Background: Neutropenia during chemotherapy has been reported to be a predictor of better survival in patients with several types of cancers, although there are no reports in pretreated patients.

Methods: We retrospectively analyzed 242 patients with advanced gastric cancer who received weekly paclitaxel as second-line. Baseline characteristics and neutropenia as time-varying covariates were analyzed as prognostic factors.

Results: Of the 242 patients, mild neutropenia (grade 1–2) occurred in 101 patients (41.7%) and severe neutropenia (grade 3–4) occurred in 63 patients (26.0%). The overall survival times in the absent group, mild group, and severe group were 3.9 months (95% CI, 2.7–5.2), 8.8 months (95% CI, 5.9–10.4), and 8.1 months (95% CI, 6.3–10.5), respectively. After adjusting for a multivariate Cox model with neutropenia as a time-varying covariate, hazard ratios of death were 0.61 (95% CI, 0.43–0.85; p = 0.004) for patients with mild neutropenia and 0.61 (95% CI, 0.41–0.88; p = 0.009) for those with severe neutropenia. Among the patients in landmark analysis (landmark of 3 months; median time to treatment failure of paclitaxel), mild and severe neutropenia remained significant prognostic factors with the HR for mild neutropenia in comparison to absent neutropenia of 0.60 (95% CI, 0.41–0.88; p = 0.009), and the HR for severe neutropenia in comparison to absent neutropenia of 0.63 (95% CI, 0.44–0.98; p = 0.048).

Conclusion: Our results indicate that neutropenia during chemotherapy is associated with improved survival in patients with advanced gastric cancer who received weekly paclitaxel as second-line chemotherapy. Prospective trials are required to assess whether dosing adjustments based on neutropenia may improve chemotherapy efficacy.

Disclosure: All authors have declared no conflicts of interest.

Management of Hematologic Toxicity in Patients with Advanced or Metastatic Gastric Cancer Treated with Docetaxel, Cisplatin and Fluorouracil (DCF): Results of Monocentric Experience

R. Blamonte, S. Turano, S. Palazzo

Background: Gastric adenocarcinoma is the second most common cause of cancer death worldwide. There is no standard regimen of chemotherapy for metastatic disease, although the regimen of ECF is the most used regimen, with a median survival of 7-9 months. With new regimens of chemotherapy, such as DCF, the median survival has increased, despite a major toxicities and 1-2% of toxic death.

Patients and methods: From January 2006 until December 2009 we have treated 36 chemo-naive patients with histological diagnosis of locally advanced or metastatic gastric cancer with a DCF regimen associated with prophylactic Pegfilgrastim treatment at 6th day of therapy.

Results: A total of 168 cycles were administered (median 5 per patient, range 3-8). Major responses were observed in 10 patients, with 2 complete (5.3%) and 8 partial remissions (22.2%). 16 additional pts showed disease stabilization (44.4%) and 10 progressed (27.9%). Median OS times were 12 months. Median TTP was 9.5 months. Toxicity was acceptable, worst per patient toxicities were neutropenia (grade 3-4 in 15%), febrile neutropenia (11.1%) diarrhea (grade 2 in 25%, grade 3 in 25%, grade 4 in 18%), asthenia (grade 2 in 48%, grade 3 in 4%), nausea (grade 4 in 10%), four pts received blood transfusion.

Conclusion: DCF scheme in locally advanced or metastatic gastric carcinoma is one scheme that provides good results both in terms of Time to Progression or Overall Response Rate and that has an acceptable toxicity even in not highly selected patients.

Disclosure: All authors have declared no conflicts of interest.

An Artificial Neural Network for Predicting Recurrence in Patients with Distal Gastric Adenocarcinoma Underwent Gastrectomy

F. Sadeghi, M. Moghimi, S. Marashi, T. Salehiyan, H. Peyrav

Background: Surgical treatment of gastric cancer has been universally recognized as the most effective way of treatment. However, even when a cure is possible, recurrences are common. At present, it is still impossible to make reliable predictions of recurrence of the tumor. Purpose: The aim of our study was to determine whether artificial neural networks (ANNs) could be used to predict local recurrence following gastrectomy in patients with distal gastric adenocarcinoma.

Methods and materials: A total of 66 patients underwent total (35 patients) or subtotal (31 patients) gastrectomy for early adenocarcinoma of the antrum were included in our prospective nonrandomized controlled trial. The patients were followed up with a mean duration of 77.7 months (range from 1 to 85 months). Recurrence was assessed using computed tomography scans and clinical symptoms. For constructing the predictive neural network, the cases were divided into a model development (47 patients) and validation group (19 patients). By using a multilayer perceptron neural network with one hidden layer, patients’ variables including age, gender, type of surgery (total or subtotal), length of hospital stay after the surgery, and 5 measures of quality of life (QoL) following surgery were used to predict the local recurrence of the tumor.

Results: The ANN predicted the recurrence with the sensitivity of 89% and specificity of 100%. Positive and negative predictive values were 86% and 95%, respectively. Overall Qol was the best predictive variable with the importance of 0.220 in the model. The ability to work 1 month after surgery was the second most important predictive indicator (importance=0.171).

Conclusions: The results show that artificial neural networks can accurately predict the recurrence of the distal gastric adenocarcinoma in patients underwent surgery. Qol after surgery would be the best predictor of the recurrence.

Disclosure: All authors have declared no conflicts of interest.

Serum LDH Level as a Prognostic Factor for the Patients with Advanced Gastric Cancer

H.B. Lee1, S.I. Lee2, Y.J. Yu3

Background: Though serum LDH level is frequently elevated in the patients with advanced gastric cancer, its clinical significance is still elusive. Moreover, the relationship between the change of serum LDH level after chemotherapy and the response to the treatment has not been studied, yet. We analyzed serum LDH level as a prognostic factor for the patients with advanced stomach cancer.

Methods: We assessed serum LDH level before chemotherapy for the patients who were planned to receive palliative chemotherapy. We re-assessed their serum LDH level at the time when the response to chemotherapy was evaluated after 2-4 cycles of treatment. The survival duration and the response to chemotherapy for the patients with low serum LDH level were compared to the survival duration and the response to chemotherapy for the patients with high serum LDH level. The relationship between the change of serum LDH level and the response to the treatment was evaluated, too.

Results: Total 118 patients were entered into this study and 114 patients were evaluable for their response to chemotherapy. Pre-treatment serum LDH level was normal in 88 patients and elevated in 30 patients. The response rate in the patients with high serum LDH level was significantly higher than the response rate in the patients with normal serum LDH level (54.5% versus 15.3%, p < 0.003). However, the patients with normal serum LDH level lived longer than the patients with high serum LDH level (median: 378 days versus 206 days, p < 0.001). The normalizing of the elevated serum LDH level after chemotherapy was related to the good response to treatment (response rate 50.0% versus 18.8%, p < 0.05).

Conclusion: For the patients with advanced gastric cancer, high serum LDH level was related to better response to chemotherapy but shorter survival duration. The normalization of elevated serum LDH level after chemotherapy was related to good response to treatment.

Disclosure: All authors have declared no conflicts of interest.

Prognostic Significance of S100A4 Expression in Curatively Resected Stage IV Stomach Cancers

J.Y. Cho1, E.M. Nam2, K.E. Lee2, Y.C. Mun2, C.M. Seong2, S.N. Lee2, J.H. Lee3, Y.J. Kim4

Background: Stage IV stomach cancers were still incurable disease and have a poor prognosis. However, limited cases of resectable stage IV stomach cancer could be cured and showed long-term survival. S100A4, a member of calcium-binding protein, was known as a metastasis related genes and correlated with cancer invasion and metastasis. We investigate the role of S100A4 expression as a prognostic marker in patients with curatively resected stage IV stomach cancer.

Disclosure: All authors have declared no conflicts of interest.
Results: The median age was 70 years with a male-to-female ratio of 1.5:1. No differences in age and sex between the HER2-positive and HER2-negative groups were found. Seventeen cases were located in the gastroesophageal junction (GEJ) and 83 were located in the stomach. Overexpression of HER2 was detected in 9 (9%) of 100 GC patients. Eight patients had IHC3+ and one IHC2+ had FISH+. From the HER2-positive group, all cases were of intestinal type. One case was stage II, five cases stage III and three cases stage IV. The overexpression rate of HER2 in stage III/IV disease was significantly higher than that in stage I/II disease (15% vs. 3%, p=0.045). Five cases (56%) were localized in the GEJ and the other four (44%) were primarily gastric. HER2-positive rates according to tumor location were higher in GEJ than in GC (33% vs. 5%, p=0.005). Survival data is not yet available.

Conclusions: HER2-positive in Peruvian patients with metastatic GC displays a similar heterogeneous staining to that reported in the ToGA study. Patients with primary disease in the GEJ had higher rates of HER2-positivity. The HER2 positivity rate was also higher in advanced stages suggesting its late role in GC oncogenesis.

Disclosure: All authors have declared no conflicts of interest.

778 IMMUNOHISTOCHEMICAL EXPRESSION OF HER2 IN LIMITIS PLASTICA-TYPE GASTRIC CARCINOMA


Background: HER2 overexpression in gastric cancer has become an important target of treatment in gastric carcinoma since the TOGA trial’s results. In this study as in some other, HER2 expression was highly correlated with histologic subtype, reported as significantly higher in intestinal than diffuse type. The aim of our study was to evaluate the frequency of HER2 expression in a homogeneous group of diffuse, limitis plastica gastric carcinoma (LPGC) and to report clinicopathological characteristics, treatment regimen, prognosis factor and survival rates.

Patients and methods: 305 cases of patients with gastric carcinomas consecutively treated between 2003 and 2009 were reviewed. Among them, 55 cases of diffuse, LPGC were identified. The histological type of the tumors was determined according to Lauren’s criteria and WHO classification. HER2 expression was determined by IHC with monoclonal antibody (Hercept Test) on paraffin-embedded tumor specimen. Overexpression of the HER2 protein was defined as a 3+ positivity with IHC. Gene amplification by FISH was determined when IHC was 2+ positive.

Results: Twenty patients (36.3%) were male and 35 (64%) female. Age ranged from 27 to 85 years, with a median value of 55.7 years. The median follow-up was 1 year. Metastasis was initially present in 39 patients (70.9%). Curative-intent surgery was done in 24 patients (44%) except one who had a partial gastrectomy as a palliative procedure. R0 resection (curative resection with no residual) was achieved in 19 cases and a mean number of 9 lymph nodes were retrieved (range 2-37). 15 patients (27%) received radiotherapy, 11 of them (73%) on adjuvant bases. Therty two (58%) patients received palliative chemotherapy in a metastatic status. The median overall survival for the entire population was 32 months. The survival rates at 12 months were 70% for overall (OS) and 55% for disease free survival (DFS) rates. In a preliminary analysis (20 patients tested), none of the gastric tumors were HER2 positive.

Conclusion: According to the results of our study, LPGC proved to be extremely aggressive histological form, characterized by reduced rate of survival. We confirmed a low rate of HER2 overexpression in this particular group of patients.

Disclosure: All authors have declared no conflicts of interest.

779 USEFULNESS OF STAGING LAPAROSCOPY AND INDUCTION CHEMOTHERAPY WITH S-1 PLUS DOCETAXEL FOR ADVANCED GASTRIC CANCER

S. Iwagami 1, M. Iwastuki 1, N. Hayash1, M. Watana1, H. Baba2

1Department of Gastroenterological Surgery, Kumamoto University, Kumamoto, JAPAN, 2Kumamoto University Hospital, Kumamoto, JAPAN

Background: The prognosis of gastric cancer patients with peritoneal metastasis is poor. Therefore, evaluation of the peritoneal metastasis is important to decide the treatment strategy for patients with advanced gastric cancer. Recently, chemotherapy with S-1 based combination therapy has been shown to be highly effective for advanced gastric cancer.

Patients and methods: Between July 2007 and December 2009, staging laparoscopy was performed for 24 patients with advanced gastric cancer at Kumamoto University Hospital. Eleven of 24 patients (46%) had either macroscopic or microscopic peritoneal dissemination and were received induction chemotherapy. The response of peritoneal metastasis to the induction chemotherapy, adverse events and the outcome of the following surgery were retrospectively evaluated.

Results: The median age was 65.4 years (range, 39–80 years). There were 18 men and 6 women. The number of patients with type2, 3, and 4 tumors were 4, 14, and 6 respectively. The mean tumor size was 9.4cm (range, 3.0–20cm). Clinical staging before staging laparoscopy was stage II in 5 patients, stage IIIA in 8, stage IIIB in 16, and stage...
TREATMENT FOR PATIENTS WITH CYTOLOGY POSITIVE AND/OR PERITONEAL DISSEMINATION FROM GASTRIC CANCER IN OUR HOSPITAL

1Cancer Therapy Center, Osaka Medical College, Takatsuki/JAPAN, 2Chemotherapy Center, Osaka Medical College, Takatsuki/JAPAN, 3Internal Medicine A, Osaka Medical College, Takatsuki/JAPAN, 4Surgery, Osaka Medical College, Takatsuki/JAPAN

We retrospectively assessed the survival benefit of surgery for patients with cytology positive and/or peritoneal dissemination from gastric cancer. Methods: From 2008 to 2010, 51 patients with cytology positive and/or peritoneal dissemination form gastric cancer visited chemotherapy center after surgery. We evaluate the surgical procedure and prognosis. Result: Gastrectomy was performed in 31 ( Cure B:cases, Cure C27:cases) of 51 patients. Only staging laparoscopy or gastroscopy was performed 20 of 51 patients. Two of 51 patients couldn’t receive first line chemotherapy due to rapid progression after surgery. Forty two patients received oral fluorouracil-based chemotherapy (S-1 alone:21cases, S-1+CDDP:12cases, S-1+CPT-11:cases, Others:cases) Seven patients received infusional chemotherapy (CPT-11+CDDP:cases, S-FU:cases). The median survival time was not significantly prolonged in gastrectomy group compared non-gastrectomy group. Conclusion: Multivariate analysis showed that received S-1+CDDP was the factor that contributed to survival time. Conclusion: The survival time of patients with cytology positive and/or peritoneal dissemination from gastric cancer was prolonged by the chemotherapy with S-1+CDDP but no significant prolongation was observed in the patients with gastrectomy. Disclosure: All authors have declared no conflicts of interest.

INFORMATIVITY OF SEROLOGICAL ONCOASSOCIATED MARKER CA 72-4 IN EARLY DIAGNOSTICS OF GASTRIC CANCER RECURRENCE

M.S. Khudayberdieva1, M.D. Djuraev2
1Gynaecology, National Oncology Centre of Uzbekistan, Tashkent/UZBEKISTAN, 2Abdominal, National Research Center of Oncology, Tashkent/UZBEKISTAN

Background: to study the value of oncomarker CA 72-4 in early diagnostics of gastric cancer recurrence. Materials and methods: There examined 70 patients with gastric cancer recurrence. Radical surgery was performed on 15 (21.4%) patients, and 55 (78.6%) unresectable patients received 2-3 cycles of chemotherapy by ELF and FAP regimens. Study was carried out on an empty stomach in dynamic order before and after therapy. Concentration oncomarker in blood up to 6.9 u/ml is considered to be a normal value. Results: Oncomarker examination after radical surgery in 15 patients showed that in 8 (53.3%) patients oncomarker regression was from 42.4 u/ml up to 10.3 u/ml. In 7 (46.7%) patients oncomarker regression was from basic 42.4 u/ml to 10.3 u/ml. Surgery is likely to have conditionally radical character in 7 patients. Oncomarker examination was in normal in 8 patients 2 weeks after 2nd cycle of chemotherapy, but in 7 patients who were noted some increase of CA 72-4, it was decreased up to norm in 2 patients, no changes were in 3 patients and in 2 patients rise of CA 72-4 level was found. Micrometatases is likely to be eliminated in 2 patients in whom CA 72-4 decreased up norm, but 5 patients chemotherapy effect was restricted or was not followed at all. 55 (78.6%) patients received chemotherapy. CA 72-4 level was at the average 40.3 u/ml before chemotherapy cycle administration. However, CA 72-4 in repeated studies were made in 46 (83.6%) patients. According to dynamics of level patients might be divided in 3 groups: First group – 12 patients, in whom CA 72-4 regression was from basic up to 22.2 u/ml and by WHO recommendations partial regression of tumor process was noted. In second group – 16 patients CA 72-4 regression at the average was 31.2 u/ml and it was noted stabilization of the process. In third group – 18 patients, despite they received 2 cycle of chemotherapy, CA 72-4 level was considerably risen and at the average was up to 49.3 u/ml here the tendency to progressing was detected. Conclusion: CA 72-4 study has a large prognostic value not only in early recurrence occurrence but also is an important biological criterion for definition of radical surgery. Disclosure: All authors have declared no conflicts of interest.
Aim: The aim was to assess the pre-operative body composition (BC) status (i.e. weight and components of weight) in patients recetible ductal pancreatic adenocarcinoma (PCa) presenting for a Whipple’s Procedure (WP) and to relate these findings to histopathology and long term survival.

Methods: BC was measured one day pre-operatively in 36 patients (15 M, 21 F), aged 41 to 81 years. Results of Total Body Protein (TBP), Total Body Water (TBW), Fat Mass (FM), and Total Body Potassium (TKB; an indicator of Lean Body Mass) were compared with those of age- and sex-matched controls. Patients’ survival and detailed histopathology synoptic reports were documented.

Results: BC: Compared with age- and sex-matched controls, the WP patients had lower TKB (P=0.001). In addition, the body fat was shown to be lower in female (P=0.007) but not in the cohort of male patients. Two of 36 (3%) patients had unclear margins and were found to have, compared with the clear margin group, larger tumours and reduced weight (P=0.015), FM (P=0.011), TKB (P=0.045), TKB (P=0.014), TBW (P=0.019) and survival (P=0.036). Histopathology: There were strong correlations between margin involvement and tumour size (P=0.018). Also, vascular invasion was associated with tumour size, (P=0.033), tumour grade (P=0.008) and nodal involvement (P=0.044). Survival: Of the BC parameters tested only FM (P=0.09) predicted survival. Analysis of the pathological parameters indicated that vascular invasion (P=0.001) and margin status (P=0.013) independently predicted survival. There were no significant differences between clear and unclear margin groups in their length of hospital stay.

Conclusions: In comparison with controls, PCa patients had reduced TKB and FM, and the unclear margin subgroup had lower weight and all components of weight. Although, FM was a predictor of survival, the histopathological parameters were stronger predictors of survival. Hence, when a patient presents with significant weight loss, one should be alerted to the association with a more advanced cancer, and surgical treatment should be applied if the radiological characteristics indicate that clear margins can be achieved.

Disclosure: All authors have declared no conflicts of interest.

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**Aims:** The aim was to assess the pre-operative body composition (BC) status in patients with metastatic cholangiocarcinoma (MCa). The BC parameters were compared with those of age- and sex-matched controls. Patients’ survival and detailed histopathology synoptic reports were documented.

**Results:** BC: Compared with age- and sex-matched controls, the MCa patients had lower Total Body Potassium (TKB; an indicator of Lean Body Mass) (P=0.001). In addition, the body fat was shown to be lower in female (P=0.007) but not in the cohort of male patients. Two of 36 (3%) patients had unclear margins and were found to have, compared with the clear margin group, larger tumours and reduced weight (P=0.015), Fat Mass (FM) (P=0.011), TKB (P=0.045), TKB (P=0.014), TBW (P=0.019) and survival (P=0.036). Histopathology: There were strong correlations between margin involvement and tumour size (P=0.018). Also, vascular invasion was associated with tumour size, (P=0.033), tumour grade (P=0.008) and nodal involvement (P=0.044). Survival: Of the BC parameters tested only FM (P=0.09) predicted survival. Analysis of the pathological parameters indicated that vascular invasion (P=0.001) and margin status (P=0.013) independently predicted survival. There were no significant differences between clear and unclear margin groups in their length of hospital stay.

**Conclusions:** In comparison with controls, MCa patients had reduced TKB and FM, and the unclear margin subgroup had lower weight and all components of weight. Although, FM was a predictor of survival, the histopathological parameters were stronger predictors of survival. Hence, when a patient presents with significant weight loss, one should be alerted to the association with a more advanced cancer, and surgical treatment should be applied if the radiological characteristics indicate that clear margins can be achieved.

**Disclosure:** All authors have declared no conflicts of interest.
PHASE II STUDY OF FIXED DOSE-RATE INFUSION OF GEMCITABINE AND UFT COMBINATION CHEMOTHERAPY IN PATIENTS WITH ADVANCED BILE DUCT CANCER: DAEGU GYEONGBUK ONCOLOGY GROUP

1Internal Medicine, Daegu Catholic University Hospital, Daegu/SOUTH KOREA
2Hematology-Oncology, Yeungnam University Hospital, Daegu/SOUTH KOREA
3Internal Medicine, Yeungnam Univ Medical Center, Daegu/SOUTH KOREA
4Hemat-Oncology, Dongsan Medical Center, Daegu/SOUTH KOREA
5Oncology/Hematology, Kyungpook National University Hospital, Daegu/SOUTH KOREA
6Internal Medicine, Daegu Fatima Medical Center, Daegu/SOUTH KOREA

Purpose: This phase II study evaluated efficacy of fixed dose rate (FDR) infusion of gemcitabine (10mg/m2/min) and UFT combination in chemo-naïve patients with advanced bile duct cancer.

Patients and methods: This was an open-label, single-arm, multicenter, phase II study with a Simon two-stage minimax design. Patients received the FDR gemcitabine 1000mg/m2 for 3 consecutive weeks and UFT 400mg/m2 on days 1-21. The cycle was repeated every 28 days. The primary end point was Response Evaluation Criteria in Solid Tumors (RECIST)-defined objective response rate. Secondary end points included clinical benefit response (CBR), safety, progression-free survival (PFS), and overall survival (OS). Clinical characteristics including four single nucleotide polymorphisms in DNA repair genes (RecQ, RAD51, XRCC1, ATM) were evaluated whether these influence the overall survival.

Results: Between December 2006 and February 2008, fifty-one patients were enrolled, with a median age of 58 years. The majority of patients (76%) had intra-hepatic disease. Fourteen patients (27%) had a RECIST investigator-assessed, partial response (PR); disease control rate (PR + stable disease) was 55%. CBR was 14% among 37 evaluable patients. Hematologic toxicity was main grade 3 or 4 treatment-related adverse events. Median PFS was 4.0 months (95% CL, 2.9 to 5.1 months). Median OS was 7.0 months (95% CL, 5.5 to 10.5 months). Intrahepatic disease, poor performance, and, and, XRCC1 R194W C/C type were predictive markers of poor overall survival.

Conclusion: FDR gemcitabine demonstrated apparent activity in patients with advanced bile duct cancer. However, this activity did not translate to prolong survival. The location of disease, performance status, and, and, polymorphic variants of DNA repair genes may affect clinical outcome of patients with advanced bile duct cancer.

Disclosure: All authors have declared no conflicts of interest.

A PHASE I/II TRIAL OF CONTINUOUS HEPATIC INTRA-ARTERIAL INFUSION OF 5-FUOROURACIL, MITOXANTRONE AND CISPLATIN (FMP THERAPY) FOR ADVANCED HEPATOCELLULAR CARCINOMA

M. Ikeda1, T. Okuzaka2, Y. Sato3, J. Furuse4, K. Nakachi1, H. Ueno2, C. Morizane5, Y. Inatomi5, M. Satake6, Y. Arai7
1Division of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital East, Kawasaki/JAPAN, 2Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital, Tokyo/JAPAN, 3Akita Cancer Center Hospital, Akita/JAPAN, 4Medical Oncology, Kyorin University School of Medicine, Mitaka/JAPAN, 5Department of Interventional and Diagnostic Radiology, Aichi Cancer Center Hospital, Nagoya/JAPAN, 6Division of Diagnostic Radiology, National Cancer Center Hospital East, Kawasaki/JAPAN, 7Division of Diagnostic Radiology, National Cancer Center Hospital, Tokyo/JAPAN

Background: The aim of this study was to investigate the maximum-tolerated dose and determine the recommended dose, based on the frequency of dose-limiting toxicities, of continuous hepatic intra-arterial infusion of 5-fluorouracil, mitoxantrone and cisplatin (FMP therapy) in a phase I study protocol, and to evaluate the efficacy and toxicity of FMP therapy at the recommended dose for advanced hepatocellular carcinoma (HCC) in a phase II study protocol.

Methods: Forty-five patients with advanced HCC who were not candidates for surgical resection, local ablation or transcatheter arterial embolization, had no history of prior chemotherapy, were enrolled. The therapy consisted of intra-arterial administration of cisplatin (P) and mitoxantrone (M) on day 1, and continuous intra-arterial infusion of 5-fluorouracil (F) from day 1 through day 5 (F/M/P[mg/m2]: Level 1; 400/4/60, Level 2; 500/6/60, Level 3; 600/6/60). The treatment was repeated every four weeks for a maximum of six courses, until the appearance of evidence of tumor progression or of unacceptable toxicity.

Results: In the phase I part of the study, one of six patients at level 1 developed DLT, including grade 3 pulmonary embolism, while none of the patients at either level 2 or 3 exhibited any signs of dose-limiting toxicity. Therefore, the recommended dose of FMP therapy was determined to be the level 3 dose. In the phase II part, 36 patients were enrolled. Nine patients (25%) achieved a partial response, and the response rate was 25% (95% confidence interval: 12-42%). The overall median survival time, 1-year survival rate and median progression-free survival were 11.3 months, 46.9% and 7.0 months, respectively. The main grade 3 and 4 hematological and non-hematological toxicities were leucopenia (36%), neutropenia (19%) and thrombocytopenia (19%), and elevation of the serum levels of aspartate aminotransferase (22%) and alanine aminotransferase (14%). These toxicities were generally transient and well-tolerated.

Conclusion: In patients with advanced HCC, hepatic arterial infusion of FMP was feasible, however, no favorable tumor response or survival benefit could be demonstrated.

Disclosure: All authors have declared no conflicts of interest.
DEEP ELECTRO-HYPERTHERMIA WITH OR WITHOUT THERMO-ACTIVE DRUGS: OUR EXPERIENCE IN PATIENTS WITH ADVANCED HEPATIC CELL CARCINOMA (HCC)

OncoMedica Speciali Civili, Oncologia-Fondatazione Beretta, Brescia/ITALY

Until 2008 advanced HCC has no standard chemotherapy. We evaluated effectiveness and toxicity of capacitatively coupled low-frequency 13.56 MHz deep hyperthermia (EHY) 2000 treatment on HCC which underwent all other possible treatment.

Methods: From 02/2005 to 09/2009, we enrolled 63 pts with advanced HCC. Median age was 69 y (range 61 -78), pts male/female were 53/10. 47.6% of pts had metastasis (11% bone retroperitoneal, peritoneal, soft tissue, lung, 26.8% node, 38.1% portal vein thrombosis). 19 pts underwent only to EHY owing to clinical conditions. Schedule: EHY was achieved by arrangements of capacitative electrodes with a radiofrequency field of 13.56 MHz (RF-DHT) at 80-130 W equivalent to 41 - 47 °C for 60 minutes, 2 times/week for 5 weeks plus thermo-active agents. (TAA), EHY was applied over 2 time a week or 1 hour as mono - combined therapy . TAA was oxiplatin 50 mg at fixed dose on D 1 and D 15 in 15% of pts or cisplatin 20 – 25 mg at fixed dose/w or 5 administrations in 54% of pts. 10 applications of EHY are 1 cycle, Median number of cycles was 1.5 (range 1-4), total EHY applications were more than 65.

Results: EHY plus TAA had clinical benefit with an excellent compliance on out-patients. We observed 1 CR, PR, 36%, 36% of SD. Median survival time was 7.5+ (range 1 – 62) months for pts at 96.9 months in pts with portal thrombosis. 16 pts presented evidence of increasing well-being: someone stopped or reduced analgetic therapy or they referred a reduction of anxiety. OS after 6 mths is 46% (29 pts). at 1 year 13.1 % (8 pts). Toxicity: only 6 pts had skin reaction . 3 pts treated with medium diameter deblowed cutaneous hyperemia on the area of treatment and mild dryness on the Skin; all symptoms disappeared after local steroid therapy , EHY was stopped until resolution.

Conclusions: Clinical benefit and Low toxicity will be confirmed in further clinical studies. Capacitatively coupled low-frequency 13.56 EHY is feasible for chemoablative HCC.

Disclosure: All authors have declared no conflicts of interest.

IMPACT OF DIFFERENT PATIENT MANAGEMENT APPROACHES ON THE CONTROL OF CAPECITABINE-RELATED ADVERSE EVENTS: A PROSPECTIVE COHORT ANALYSIS FROM SAEDA II

R. Winterhalder1, G. Delmore2, P. Hösl3, A. Hügi-Dayer4, M. Mannhart5, F. Otto6, S. Pederiva7, M. van Lier8, S. Nick9, R. Winterhalder9
1Department of Oncology, Kantonsspital Graubünden, Chur/SWITZERLAND, 2Department of Oncology, Kantonsspital Luzern, Luzern/SWITZERLAND, 3Department of Oncology, Kantonsspital Bregenz, Bregenz/SWITZERLAND, 4Department of Oncology, Kantonsspital St. Gallen, St. Gallen/SWITZERLAND, 5Department of Oncology, Kantonsspital Winterthur, Winterthur/SWITZERLAND, 6Department of Oncology, Kantonsspital Zug, Zug/SWITZERLAND, 7Oncology, Kantonsspital Andelfingen, Andelfingen/SWITZERLAND, 8Roche Pharma (Schweiz) AG, Reinach/SWITZERLAND, 9Kantonsspital Graubünden, Chur/SWITZERLAND

Background: A previous cohort analysis showed high compliance with capecitabine independent of age or ECOG status [SAEDA I; Winterhalder et al. ASCO GI 2009]. This prospective cohort analysis of patients receiving capecitabine-based chemotherapy aimed to identify patient management approaches to improve adverse-event (AE) control, which may further increase compliance and therapeutic outcome.

Methods: From 02/2005 to 09/2009, we enrolled 63 pts with advanced HCC. Median age was 69 y (range 61 -78), pts male/female were 53/10. 47.6% of pts were un-eligible (including reasons) were collected at each of 6 consecutive visits and adverse events were documented for all pts. Compliance was assessed with a compliance diary, pill box and patient AE-information card.

Results: In this final analysis, 52 physicians provided data on 243 patients (40% male) receiving capecitabine-based therapy, of which 55% had colorectal, 23% breast, 10% other primary tumours. Compliance was high (90%) and was independent of age and ECOG status. Most frequent AEs were nausea/vomiting, hand-foot-syndrome (HFS), diarrhea and loss of appetite. Non-compliant patients had a higher rate of nausea (54% vs 43%), vomiting (16% vs 14%) and depression (15% vs 3%) than compliant patients. Elderly patients (<65 vs 78 yrs) had more side effects than the younger patients (<65, 1.74 vs 1.49; ≤70, 1.66 vs 1.51), mainly due to higher rates of nausea/vomiting. Of the patient support provided patients received >20 min of patient education dialogue had less AEs than those with <20 min (1.49 vs 1.84). In addition, patients using patient diaries had a better rate of AE-control (1.40 vs 1.68). No impact was observed from patient brochures, tablet box or a patient AE-information card.

Conclusions: This final analysis indicates that patients are highly compliant with capecitabine, irrespective of age and ECOG status. Compliance is negatively influenced by nausea, vomiting and loss of appetite, which interact directly with the oral application of the medication. Doctors actively providing patient support are more successful in the control of AEs. The total time spent on patient education and patient diaries can improve AE control.

Disclosure: R. Winterhalder: Consultant / advisory board member for F. Hoffmann-La Roche. M. van Lier: Employee, product manager, F. Hoffmann-La Roche. S. Nick: Employee, medical manager, F. Hoffmann-La Roche. R. von Moos: Compensated consultant / advisory board member for F. Hoffmann-La Roche, Amgen, Novartis Speaker honoraria from F. Hoffmann-La Roche, Amgen. M. van Lier: Employee; product manager, F. Hoffmann-La Roche. S. Nick: Employee; medical manager, F. Hoffmann-La Roche. R. Winterhalder: Consultant / advisory board member for F. Hoffmann-La Roche. All other authors have declared no conflicts of interest.
#### TRENDS IN GASTROINTESTINAL CANCER REFERRALS IN ACUTE HOSPITALS IN LONDON, UK

**M. Cheng, A. Jamil**
Medicine, East Kent University Hospitals NHS Trust, Ashford/UNITED KINGDOM

**Introduction:** Upper gastrointestinal (UGI) and lower gastrointestinal (LGI) cancers accounted for 6% and 12.5% of 10 commonest cancers occurring in the UK and Ireland during the 1990s. Although there is little geographical variation in incidence and mortality for all cancers combined, there appears to be some variation for certain types of cancer.

**Aims and methods:** To analyze trends in the number of suspected UGI and LGI cancer referrals for all London Acute NHS Hospitals Trusts (AHT) between 2007-2008.

**Results:** Forty three (55%) of the 78 analysed patients were male. The mean age was 56.3. The majority of the primary tumors were localized in the abdominal viscera (72%) (5/6). The most encountered primary tumor site among those was pancreas (28% - 22). Other primary tumor sites according to their frequency follows as stomach (24% n=19), gall bladder (%12 n=9) and small intestine (7.6% n=6). The remainder primary tumor sites show a wide range of distribution, including breast carcinoma, synovial sarcoma and malignant melanoma. The most common histological type was adenocarcinoma (67%, n=52). Most of the patients received diagnostic surgical procedures; definitive procedures as such liver resection were possible only in 26 patients (34%). More than half of the patients who underwent liver resection had gastric cancer.

**Discussion:** Liver resection should be kept as an option in case of long disease free survival and solitary metastases in non colorectal liver metastases.

**Disclosure:** All authors have declared no conflicts of interest.

#### TRENDS IN GASTROINTESTINAL CANCER REFERRALS IN ACUTE HOSPITALS IN LONDON, UK

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with fluoropyrimidine toxicity in the adenin setting of colon and gastric cancer patients.

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#### PHASE II STUDY OF GEMCITABINE AND OXALIPLATIN IN UNRESECTABLE GALL BLADDER CANCER

**M. Uddin1, A. A. Hannan2, I. Ahmed3**
1Department of Radiotherapy, Rajshahi Medical College and Hospital, Rajshahi/ BANGLADESH, 2Surgery, Rajshahi Medical College and Hospital, Rajshahi/ BANGLADESH, 3Rajshahi Medical College and Hospital, Rajshahi/ BANGLADESH

**Purpose:** Oxaliplatin and Gemcitabine are active in the treatment of Advanced Gastrointestinal tract malignancy. We conduct a phase II study to evaluate efficacy and safety of Oxaliplatin and gemcitabine combination in unresectable Gall Bladder Cancer. Design Drugs gemcitabine 1000 mg/m² on day 1 and oxaliplatin 85 mg/m² IV infusion on day 2, 3-weeks cycle for a maximum of six cycles or unacceptable toxicity which ever was earlier.

**Materials and methods:** Thirty five patients were enrolled and analysis was restricted to 34 who were treated. Median age was 42 years and 21 patients were females.

**Results:** 12 patients (35%) survived for a year or more. There was no toxic death and grade III/IV toxicity seen in 10 (29%) patients: diarrhea 3, vomiting 2, neutropenia and thrombocytopenia 5 patients.

**Conclusion:** This combination of Oxaliplatin and Gemcitabine is effective in unresectable GBC. It need further evaluation in large population to be considered as a new treatment option of unresectable gall bladder cancer.

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#### PHASE II STUDY OF GEMCITABINE AND OXALIPLATIN IN UNRESECTABLE GALL BLADDER CANCER

**M. Uddin1, A. A. Hannan2, I. Ahmed3**
1Department of Radiotherapy, Rajshahi Medical College and Hospital, Rajshahi/ BANGLADESH, 2Surgery, Rajshahi Medical College and Hospital, Rajshahi/ BANGLADESH, 3Rajshahi Medical College and Hospital, Rajshahi/ BANGLADESH

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**Disclosure:** All authors have declared no conflicts of interest.

#### A RETROSPECTIVE ANALYSIS OF GALLBLADDER CANCER PATIENTS REFERRED TO THE NATIONAL CANCER INSTITUTE IN MEXICO BETWEEN 2004-2009

**E. Ruiz-García1, G. Calderillo-Ruiz1, G. Astudillo-De la Vega2, R. Martinez1, C. P. Izaguirre1, J. L. Aguilar Ponce1, N. Reynoso-Noverón1**
1Medical Oncology Unit, Instituto Nacional de Cancerología, Mexico City/ MEXICO, 2Translational Research and Cell Therapy Laboratory, IMSS, Mexico City/MEXICO, 3SCD Epidemiology, Secretaria de Salud, Mexico City/MEXICO

**Introduction:** Gallbladder cancer is the most common malignant tumor of the biliary tract. It is associated with a desolate prognosis, with a 5-year survival rate of 5%. There are some parts of the world where the incidence is comparatively high, contributing to a health problem as a result of its associated poor outcome. All the statistics mentioned above comes from developed countries. We decided to do this research to know what is happening in our country, specifically in our hospital.

**Methods:** A retrospective analysis of gallbladder cancer patients referred to the National Cancer Institute in Mexico from 2004 to 2009 was performed. For the analysis we used SPSS version 17.

**Results:** 46 patients were identified. The mean age was 61.5 years (range 55-80). Most of the patients were female (71.7%). 89.1% were adenocarcinoma meanwhile 10.9% were squamous. According to TNM there were 8 cases stage I, 41.3% stage II, 2.2% and 43.5% stage III and IV respectively. Two cases were not classified. Mean time from...
the beginning of the symptoms and the first giving treatment was 220 days (range 102-338). We examined different prognostic factors for overall survival finding that only albumin levels were significant (95% IC 0.098-.765; p=0.013) Figure 1. Serum alkaline phosphatase was significantly elevated in 63% of patients (from 127 until 1182 U/L). Gallbladder cancer was incidentally found in thirty three patients during cholecystectomy (71.7%), none of these were re-explored. 39% of the patients were treated with palliative chemotherapy, 21% to palliative radiotherapy meanwhile 24% with the best support care. In our Institution, the initial treatment was performed only in 21% of all cases (n=15), notice that 60% were stage IV. From this subgroup, 60% received a palliative treatment with chemo or radiotherapy, and 40% with just the best support care.

Conclusion: A high percentage of our patients have been initially treated by a non oncologist surgeon, and/or come to our institution with an advanced disease. We found out that most of them presented decreased serum albumin levels (<3.5 g/dl) and we suggest that this is an adverse prognostic factor for overall survival.

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