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upper gastrointestinal tumors

1071O A PHASE III TRIAL COMPARING ADJUVANT CHEMOTHERAPY TO CHEMORADIOTHERAPY IN OPERABLE GASTRIC CANCER. A HELLENIC COOPERATIVE ONCOLOGY GROUP STUDY

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Background: Adjuvant chemoradiotherapy using bolus 5FU has been established as the standard treatment of stage II/III gastric cancer. The focus of research in this area now is on optimizing the chemotherapy regimen and defining the role of radiotherapy. This study was designed to determine whether the addition of radiotherapy to chemotherapy as adjuvant treatment, translutes into an overall survival (OS) and disease-free survival (DFS) advantage in operable gastric cancer.

Patients and methods: From 8/4/2002 to 13/4/2005, 133 patients with operable gastric cancer were randomized after surgery to receive either 6 cycles of carboplatin (5 AUC) and docetaxel (75 mg/m^2) every 21 days (Group A, N=65), or the same chemotherapy regimen with an additional radiotherapy course of a total of 45 Gy, administered between cycles 3 and 4 (Group B, N=68). Analysis was performed following the intent to treat principle.

Results: Fifty three patients (81.5%) completed 6 cycles of chemotherapy in group A, while 49 patients (72%) completed chemotherapy in group B. Fifty six patients treated in group B received radiotherapy (85%). Most commonly observed severe (grade 3 and 4) toxicities were alopecia (23% in group A versus14% in group B, p=0.26), non-febrile neutropenia (12% in group A versus 19% in group B, p=0.47), febrile neutropenia (8% in group A versus 6% in group B, p=0.99) and diarrhea (11% in group A versus 1.5%, p=0.06). Median relative dose intensity for docetaxel was 0.98 for patients treated in group A and 0.96 for patients treated in group B, while the cumulative dose of carboplatin was 2850 and 2400 in the two groups respectively. After a median follow-up of 25 months, no differences between the two groups were observed, in terms of OS and DFS (p=0.76 and 0.15, respectively).

Conclusion: This study could not demonstrate a significant difference in the survival of patients with operable gastric cancer treated either with adjuvant chemotherapy alone or chemoradiotherapy.

1072O RANDOMIZED PHASE III TRIAL OF CAPECITABINE/CISPLATIN (XP) VS. CONTINUOUS INFUSION OF 5-FU/CISPLATIN (FP) AS FIRST-LINE THERAPY IN PATIENTS (PTS) WITH ADVANCED GASTRIC CANCER (AGC): SUBGROUP ANALYSES CONFIRM MAIN EFFICACY FINDINGS

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Background: The oral fluoropyrimidine capecitabine has proven efficacy and safety in colorectal and breast cancer. Phase II data in AGC suggested that XP would show comparable efficacy to a standard FP regimen, with potential safety and convenience advantages. This phase III study evaluated XP vs. FP in first-line AGC.

Methods: Pts with previously untreated measurable AGC received either oral capecitabine (1000 mg/m^2 bid d1-14) + cisplatin (80 mg/m^2 i.v. d1) q3w (XP arm) or 5-FU (800 mg/m^2/d continuous infusion, d1-5) + cisplatin (80 mg/m^2 i.v. d1) q3w (FP arm). XP requires 1 day per 3 weeks in hospital; FP requires 5 days. Pts were treated until disease progression or unacceptable toxicity. Primary endpoint: non-inferiority in progression-free survival (PFS), defined as upper limit of 95% CI of hazard ratio (HR) <1.4 (first test) and <1.25 (second test).

Results: From Apr 03 to Jan 05, 316 pts were enrolled in 46 centers/13 countries. Arms were well balanced: median age (years, range) XP (56, 26–74), FP (56, 22–73); median Karnofsky PS 80 (range 70-100) in both arms; male/female: XP (64/36%), FP (69/31%). Median no. of cycles was 5 (XP and FP). Median follow-up is 22.1 months. Primary endpoint was met: HR 0.81 (95% CI, 0.63–1.04). Overall response rate (ORR, RECIST) was superior with XP vs. FP (41 vs. 29%, p=0.03). Median PFS (5.6 vs. 5.0 months) and overall survival (10.5 vs. 9.3 months) were highly significantly non-inferior for XP vs. FP. These findings were confirmed in subgroup analyses (reflecting prior chemotherapy, gender, age, Karnofsky PS, no. of metastatic sites). The most common treatment-related grade 3/4 adverse events (XP vs. FP) were: neutropenia (16 vs. 19%), vomiting (7 vs. 9%), stomatitis (2 vs. 7%), diarrhoea (5 vs. 5%), and anaemia (5 vs. 3%). Other grade 3/4 events occurred in <5% of pts.

Conclusions: XP showed highly significant non-inferiority for PFS and significant superiority for ORR vs. FP with similar safety. Subgroup analyses confirmed these results and suggest that capecitabine should become the fluoropyrimidine of choice for AGC.

1073O META-ANALYSIS OF RANDOMIZED TRIALS: EVALUATION OF BENEFIT FROM COMBINATION CHEMOTHERAPY APPLIED IN ADVANCED PANCREATIC CANCER

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Background: Using standard chemotherapy with single-agent gemcitabine (GEM) a median survival time of around 6–7 months has been reported. A considerable number of randomised studies examined the question, whether the addition of a second cytotoxic agent might improve the prognosis. However, while progression-free survival was significantly prolonged in some of the individual studies, only one trial so far showed a signficant advantage for overall survival.

Methods: A meta-analysis was performed including 12 trials comparing GEM vs. GEM+X. The analysis comprised a total of 3687 patients and was predominantly based on published data.

Results: The meta-analysis revealed a significant survival benefit for GEM+X with a pooled hazard ratio (HR) of 0.91 (95% CI: 0.85 - 0.98, p=0.0079). The overall test for heterogeneity resulted in p=0.68 (I^2=0%). The analysis of platinum-based combinations indicated a HR of 0.83 (95%CI: 0.71-0.98, p=0.03), while for fluoropyrimidine-based combinations the HR was 0.89 (95%CI: 0.80-0.98, p=0.02). No risk reduction was observed in the group of trials combining GEM with irinotecan, exatecan or pemetrexed (HR=0.99). A meta-analysis of the trials with adequate information on performance status (PS) was performed in 1682 patients. This analysis indicated that patients with a good PS had a marked survival benefit when receiving combination chemotherapy (HR=0.76; 95%CI: 0.67 - 0.87; p<0.0001). By contrast, application of combination chemotherapy to patients with an initially poor PS appeared to be ineffective or even harmful (HR=1.08; 95% CI: 0.90 - 1.29).

Conclusions: The meta-analysis of randomised trials indicated a significant benefit when gemcitabine was either combined with platinum analogs or fluoropyrimidines. This benefit was specifically observed in good PS patients, while patients with a poor PS may rather benefit from single-agent therapy.

1074O DOES A SECOND DRUG ADDED TO GEMCITABINE (G) IMPROVE OUTCOME OVER G IN ADVANCED PANCREATIC CANCER (APC)? A POOLED ANALYSIS OF 5561 PATIENTS (PTS) ENROLLED IN 16 PHASE III TRIALS

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Background: Several attempts have been accomplished in order to improve efficacy of the gold standard Gemcitabine (G) in APC by combining such agent with both chemotherapeutics or new targeted agents. However, conflicting results are provided by phase III trials with polychemotherapy and the impact of novel ''biological'' drugs (ND) remains to be defined. Methods: All prospective phase III trials comparing single-agent G with G-based polychemotherapy regimens (poly-G) or G plus ND were considered eligible. A pooled analysis was performed and event-based relative risk ratios (RR) with 95% CI were derived through both a fixed- and a random-effect model approach, exploring OS as the primary outcome and PFS and ORR as secondary outcomes. Heterogeneity between different trials was also taken into account. Results: Sixteen trials involving 5561 pts were identified. The analysis was conducted considering five different subgroups: 1) overall population 5561 patients, 16 trials), 2)

polychemotherapy (poly)-G vs G (3682 pts, 12 trials), 3) platinum-containing poly-G (PG) vs G (768 pts, 5 trials), 4) fluoropyrimidine-containing poly-G (FG) vs G (1640 pts, 4 trials), and 5) ND-G vs G (1879 pts, 4 trials). As shown in the table, no significant differences in the primary outcome (OS) were observed in any of the five groups analyzed. Conversely, a significant advantage was evident with regard to both PFS and ORR in the overall population as well as in the P-G vs G subgroup (with both fixed- and random-effect model), although with some heterogeneity. Conclusions: Whatever drug (chemotherapeutics or targeted agents) is added to G, median survival is not improved. However, the addition of platinum compounds appears to significantly improve PFS and ORR, possibly justifying the use of platinum-based poly-G in younger and fit patients.

Study group	RR	95% CI	p	Heterogeneity
Overall population				
OS	0.95	0.85, 1.07	0.42	p=0.99
PFS	0.90	0.83, 0.97	0.007	p=0.24
ORR	1.57	1.30, 1.89	<0.0001*	p=0.01
Poly-G vs G				
OS	0.92	0.80, 1.05	0.23	p=0.99
PFS	0.87	0.79, 0.95	0.003	p=0.09
ORR	1.70	1.40, 2.07	<0.0001**	p=0.01
Poly-G vs G				
P-G vs G				
OSPFSORR	0.82	0.61, 1.12	0.22	p=0.98
PFS	0.66	0.53, 0.81	<0.0001	p=0.74
ORR	1.77	1.27, 2.45	0.001	p=0.17
Poly-G vs G				
F-G vs G				
OSPFSORR	0.90	0.72, 1.10	0.30	p=0.78
PFS	0.85	0.72, 1.01	0.06	p=0.23
ORR	1.37	0.97, 1.94	0.07	p=0.06
Poly-G vs G				
ND-G vs G				
OS	1.04	0.85, 1.28	0.7	p=0.71
PFS	0.97	0.85, 1.12	0.70	p=0.99
ORR	0.77	0.44, 1.38	0.37	p=0.96

*Significant at REM (p=0.001); **significant at REM (p=0.01).

1075PD PROGNOSTIC MODEL TO PREDICT SURVIVAL FOR PATIENTS WITH UNRESECTABLE OR METASTATIC GASTRIC ADENOCARCINOMA

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Purpose: To develop a multivariate model capable of predicting survival in patients with locally advanced or metastatic gastric adenocarcinoma.
Patients and methods: A total of 1455 patients out of 1598, who received first-line palliative chemotherapy for unresectable, recurrent or metastatic gastric adenocarcinoma between September 1994 and February 2005 were included in the analysis. Survival was the primary end point assessed. Clinical data at the time of the initial chemotherapy were collected.

Results:
Patient characteristics

	Patient # (%) (N=1455)
Age (median age, range)	54 (21 – 86)
Male sex (%)	948 (65.2)
Performance status	
0–1	1189 (81.7)
≥2	266 (18.3)
Disease status	
Locally advanced	43 (3.0)
Metastatic	1412 (97.0)
Previous gastrectomy	
Curative total gastrectomy	217 (14.9)
Curative subtotal gastrectomy	232 (16.0)
Palliative total gastrectomy	136 (9.4)
Palliative subtotal gastrectomy	110 (7.6)
Bypass surgery without gastrectomy	94 (6.5)
First-line chemotherapy regimen	
5-FU based	826 (56.8)
non-5-FU based	629 (43.2)

Conclusions: Seven poor prognostic factors for survival in gastric cancer patients receiving first-line palliative chemotherapy were identified in this study and prognostic model will be presented at the meeting.

Multivariate Prognostic Factors for Poor Survival

	Patient # (%) (N=1455)
Age (median age, range)	54 (21 – 86)
Male sex (%)	948 (65.2)
Performance status	
0–1	1189 (81.7)
≥2	266 (18.3)
Disease status	
Locally advanced	43 (3.0)
Metastatic	1412 (97.0)
Previous gastrectomy	
Curative total gastrectomy	217 (14.9)
Curative subtotal gastrectomy	232 (16.0)
Palliative total gastrectomy	136 (9.4)
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Bypass surgery without gastrectomy	94 (6.5)
First-line chemotherapy regimen	
5-FU based	826 (56.8)
non-5-FU based	629 (43.2)

1076PD CETUXIMAB PLUS WEEKLY OXALIPLATIN/5FU/FA (FUFOX) IN 1ST LINE ADVANCED GASTRIC CANCER. FIRST RESULTS FROM A MULTICENTER PHASE II STUDY OF THE AIO UPPER GI STUDY GROUP

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Background: Cetuximab and oxaliplatin-5FU/FA demonstrated high activity in first-line metastatic colorectal cancer. Here we report on the first available data from a trial assessing the efficacy of this combination in advanced gastric cancer. Methods: Pts received cetuximab 400 mg/m^2 at first infusion followed by weekly 250 mg/m^2 combined with the FUFOX regimen (oxaliplatin 50 mg/m^2 plus 5FU 2000mg/m^2 plus DL-folinic acid 200 mg/m^2 d1,8,15,22 qd36). The primary endpoint was response according to RECIST. Toxicity was reported according to NCI.CTC v3.0.
Results: From 4/05 until 03/06 we included 53 pts at 7 study centers: 13 women and 40 men; median age 63 years, range 38-80. 3 pts had irresectable locally advanced and 50 pts had metastatic disease. Immunohistochemical staining for EGFR is actually available in 27 pts. EGFR was detectable in 16 pts (59%). 23 pts are still being treated. 3/53 (6%) pts died within 60 days after inclusion. Completed reports on toxicity during the first 2 cycles of chemotherapy are available in 43 patients. Reported hematological toxicities grade 3/4 were: leukopenia 2.3%, febrile neutropenia 2.3%, and thrombocytopenia 2.3%. Grade 3/4 non-hematological adverse events were: diarrhea 25.6%, fatigue 7.0%, dyspnea 4.7%, sensory neuropathy 2.3%, and deep vein thrombosis 2.3%. Cetuximab-attributable skin-reactions occurred as follows: grade 0 18.6%, grade 1 34.9%, grade 2 41.9%, grade 3 9.3%. Response is actually evaluable in 28 patients showing an overall response rate of 64.4% including 1 complete and 17 partial responses. There were 25.0% stable diseases, and only 3 patients (10.7%) had progressive disease. Tumor response and toxicity data of all patients will be presented at the meeting.
Conclusion: The first analysis indicates a very promising efficacy and a tolerable safety and toxicity profile of the cetuximab-FUFOX regimen in advanced gastric cancer.

1077PD CETUXIMAB IN COMBINATION WITH FOLFIRI AS FIRST-LINE TREATMENT IN PATIENTS WITH UNRESECTABLE/METASTATIC GASTRIC OR GASTROESOPHAGEAL JUNCTION (GEJ) ADENOCARCINOMA: PRELIMINARY RESULTS OF FOLCETUX PHASE II STUDY

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Background: The aim of this phase II study was to evaluate efficacy and safety of cetuximab combined with FOLFIRI as a first-line treatment for advanced gastric or GEJ cancer.

Methods: Eligibility criteria were: histologically diagnosis of stomach or GEJ adenocarcinoma, unresectable/metastatic disease, EGFR+, measurable disease, no prior chemotherapy for advanced cancer. Pts received cetuximab weekly at 400 mg/m^2 *iv* loading dose, and then at 250 mg/m^2 *iv* maintenance dose, CPT11 180 mg/m^2 *iv* d1, LFA 100 mg/m^2 *iv* followed by 5FU 400 mg/m^2 *iv bolus* and 600 mg/m^2 *iv* continuous infusion 22h d1-2(FOLFIRI) every 2 weeks, for a maximum of 24 weeks, then cetuximab alone was allowed in pts with CR/PR/SD. Anti-tumor activity was assessed by CT and PET at baseline and after 6 weeks, and further by CT alone or CT and PET every 6 weeks.

Results: From November 2004 to December 2005, 49/54(90.7%) screened subjects were EGFR+, and 38 pts were enrolled in the study. Pt characteristics were: 26 (68.4%) males, 12 (31.6%) females; median age 63.5 years (39-82); median KPS 90 (70-100); 34 (89.4%) stomach, 4 (10.5%) GEJ; 18 (47.3%) prior gastrectomy; 13 (34.2%) prior adjuvant chemotherapy; 4 (10.5%) locally advanced disease, 34 (89.4%) metastatic disease. Median number of treatment weeks was: 13 (1-55). Median dose intensity was: 5FU 100% (25-100), CPT11 100% (25-100) and cetuximab 100%(80-100). At the present time, 27 pts are assessable for response and 38 for toxicity. Objective responses(RECIST) were: 4(14.8%)CR, 10 (37%)PR, e.g. 51.9% CR + PR (95% CI:33-70%), 11 (40.7%) SD. Median TTP is 6.5 months(3-15). Survival data are premature (86.8% of the pts are alive). Grade 3-4 toxicity (CTCv3.0) was: 16 (42.1%) neutropenia (1pt died of febrile neutropenia), 1(2.6%)thrombocytopenia, 2(5.3%)hypertransaminasemia, 1(2.6%)hyperbilirubinemia. Cutaneous toxicity was: 12(31.6%) gr1, 11(28.9%) gr2, 7(18.4%) gr3.

Conclusions: Combination of cetuximab and FOLFIRI appears to be active in gastric and GEJ adenocarcinoma.This treatment has been well-tolerated and the major toxicity appears to be limited to neutropenia.

1078PD PHASE II STUDY OF BEVACIZUMAB AND DOCETAXEL (AVATAX) IN METASTATIC ESOPHAGEAL AND GASTRIC CANCER

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Background: Single-agent docetaxel has a 17%-24% response rate (RR) in advanced gastric cancer. The addition of bevacizumab to standard chemotherapy has improved RRs and survival of patients (pts) with metastatic colorectal, lung, and breast cancer in randomized trials.

Methods: Pts with measurable, metastatic esophageal or gastric cancer received bevacizumab 5 mg/kg day 1 and day 15 and weekly docetaxel 35 mg/m^2 day 1, day 8, and day 15 on a 28-day cycle. Prior adjuvant therapy and 1 prior chemotherapy for metastatic disease were permitted.

Results: Thirty pts have been enrolled: median age= 59 years (40-78), male/female= 28/2, ECOG performance status 0/1= 13/17, gastric/gastroesophageal junction/ esophageal carcinoma= 6/4/20 and adenocarcinoma/squamous cell carcinoma 29/1. Sites of metastatic disease included: lymph nodes (23 pts), liver (21 pts), lung (15 pts), bone (3 pts), and other (3 pts). Most pts had received prior chemotherapy (24 pts) and prior radiotherapy (16 pts). Grade III/IV toxicity occurring in >5% of pts for all 30 pts was: fatigue= 4 pts (13%), gastrointestinal bleed= 4 pts (13%), anemia= 4 pts (13%), neutropenia= 3 pts (10%), and arterial thrombosis= 2 pts (7%). Additionally, 5 pts (17%) had grade II nail changes and 4 pts (13%) had grade II tearing. Treatment was held in 7 pts and reduced in 4 pts due to toxicity. Although no pts died during the study, 5 pts died within 30 days after study completion. Among 23 pts evaluable for response (5 were not evaluable and 2 were too early to assess), 1 complete response and 5 partial responses (ORR= 26.1%) were noted. Additionally, 7 pts (30.4%) had stable disease as their best response.

Conclusions: The regimen of weekly docetaxel and bi-weekly bevacizumab (AvaTax) was well tolerated, although the risk of hemorrhage and arterial thrombosis remains a concern. The preliminary RR in mostly pretreated pts is promising. Further accrual to 35 evaluable pts is ongoing. Supported by Genentech.

1079PD BEVACIZUMAB PLUS GEMCITABINE AND CAPECITABINE IN PATIENTS WITH ADVANCED PANCREATIC CANCER WITH ECOG PS 0/1: A PHASE II STUDY

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Introduction: Capecitabine (CAP) + gemcitabine (GEM) may prolong overall (OS) and progression-free survival (PFS) in advanced pancreatic cancer as compared with GEM alone. The anti-angiogenic agent bevacizumab (BEV), a humanised anti-VEGF monoclonal antibody produces synergistic anti-tumor effect with GEM or CAP. This multicenter, phase II trial is evaluating the efficacy and safety of BEV plus GEMCAP in patients with advanced pancreatic cancer.

Methods: Eligible patients: unresectable or metastatic pancreatic adenocarcinoma; no prior systemic therapy; ECOG PS 0/1; adequate organ function; no major surgery within 28 days and no CNS metastases. Patients received BEV 15mg/kg (day 1), GEM 1000mg/m2 (days 1 and 8) and CAP 650mg/m2 twice-daily (days 1-14) every 3 weeks until disease progression (maximum of 12 months). Response was assessed using RECIST. Adverse events were graded using NCI-CTC v3.0. Flow cytometric analysis for circulating endothelial cells (CECs) (CD31+, CD34+, CD45-) was performed at baseline and on day 3. The primary endpoint is an improvement in PFS of 1.6 months as compared with a historical value of 2.5 months with GEM alone.

Results: Thirty-two patients have been enrolled: median age 64.5 (range 38-79) years; 50% male; stage III/stage IV: 3/29. Cycles completed=170; median=5 (range=0-16). Response data are available for 27 patients. Partial responses confirmed in 6 (22%) patients; 18 (67%) achieved stable disease. Median PFS was 4.7 months (95% CI: 3.9-9.8); estimated OS 8.9 months (95% CI: 4.6-10.2). Treatment was well-tolerated. Grade 3/4 adverse events: pulmonary embolism (n=4), anemia (n=3), neutropenia (n=3), thrombocytopenia (n=3), hand-foot syndrome (n=3) and emesis (n=3). One grade 5 toxicity (haemorrhage). An improvement in QOL was observed in 12/19 (63%, 95% CI: 41%-81%) patients. CEC levels on day 3 were increased in 11/18 and decreased in 7/18 patients (p=0.2101).

Conclusions: These results suggest that the addition of BEV to GEMCAP improves PFS and QOL compared with historical data. The primary endpoint of the study is likely to be reached. (Supported by a grant from NCCN).

1080PD NCCTG PHASE II TRIAL OF BEVACIZUMAB, GEMCITABINE, OXALIPLATIN IN PATIENTS WITH METASTATIC PANCREATIC ADENOCARCINOMA

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Background: The combination of gemcitabine and oxaliplatin (GemOx) is an active regimen in pancreatic cancer. A study with the biologic agent, bevacizumab, and gemcitabine has also demonstrated significant activity. Based on these observations, the NCCTG initiated a multi-center phase II study to evaluate whether a regimen containing an active cytotoxic doublet with an active targeted agent improves 6-month survival and is tolerable in previously untreated patients with metastatic pancreas cancer.

Methods: Treatment consists of gemcitabine 1000 mg/m^2 IV over 100 minutes and bevacizumab 10 mg/kg IV given on day 1, 15; oxaliplatin 100 mg/m^2 IV is given on day 2, 16. A treatment cycle consists of 28 days. Eligibility includes: no prior chemotherapy, ECOG PS 0-2, bili< 2x UNL, AST< 5x UNL. Pts with stable full dose anticoagulation are eligible. Bevacizumab specific exclusions include no recent stroke, heart attack, embolus, tumor invasion or significant proteinuria. CT scans are obtained every 2 cycles. Treatment continues until disease progression, severe adverse events (AEs), or patient refusal. Evaluability for AEs required at least 2 cycles of data.

Results: Eighty-four pts were enrolled from 7/05 to 2/06 with the median duration of treatment at the time of analysis being 2 cycles. When considering only AEs that are at least possibly related to the study regimen, 18% of 65 evaluable patients had a maximum grade ≥ 4 adverse event. The majority were non-hematologic events. Three patients died from grade 5 events (1-gastric perforation, 1-cerebral ischemia, 1-multi-organ failure).

Conclusions: Early assessment of adverse events in this trial reveals a reasonably tolerable regimen, although the three grade 5 events indicate caution must be exercised and that analysis of the full dataset is required. Additional efficacy and toxicity data will be presented.

1081P PROGNOSIS OF SMALL BOWEL ADENOCARCINOMA TREATED WITH FOLFOX-4 OR XELOX; A MATCHED CASE CONTROL STUDY DERIVED FROM A DATABASE OF 581 PATIENTS WITH COLORECTAL CANCER

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Aim: Small bowel cancer (sbc) is a very rare disease, which basicly is treated as colorectal cancer (crc). The purpose was to compare efficiacy of chemotherapy and

prognosis for patients with adenocarcinoma of small bowel (sbc) to crc patients in both adjuvant and palliative settings.

Patients and metods: A case-control study including 13 sbc cases treated palliatively (n=7) with either capecitabine monotherapy or combined with oxaliplatin (XELOX) or receiving adjuvant 5-FU chemotherapy (FOLFOX-4) following surgery (n=6). A control group was derived from a database of 581 patients with crc by matching each case to 5 patients, according to the following six criterias: Chemotherapy regimen, stage, age, gender, performance state (PS) and lactate dehydrogenase (LDH).

Results: Response rate for sbc patients in the *palliative group* was 14% compared to 37% for crc patients (P=0.1). Median progression free survival times were 2.7 and 7.2 months (p=0.05) and median overall survival times were 8.5 and 12 months (p=0.6) for sbc and crc patients, respectively. In the *adjuvant group* the progression free survival rates were 63% and 93% (p<0.0001) after one year and 66% and 73% (p=0.4) after three years for sbc and crc patients, respectively. Overall survival rates after tree years were 80% and 87% (p=0.5) and after five years 80% and 82% (p=0.9) for sbc and crc patients, respectively. For the *entire patient populations* the progression free survival rates after one year were 50% and 65% (P=0.04) and median time to progression were 6.7 months and 31.1 months (P=0.6) for sbc and crc, respectively. Overall survival after 3 years were 55% and 61% (p=0.5) for sbc and crc, respectively.

Conclusion: Standard chemotherapy-regimes for patients with sbc seem less efficient and the prognosis worse compared to crc patients, especially in the palliative settings. However, ferm conclusions can not be drawn from the small patient population in this very rare disease. Multicentre studies is warranted to confirm these results and define the optimal chemotherapy regimes in sbc.

1082P A PHASE II STUDY OF DOCETAXEL IN COMBINATION WITH GEFITINIB IN GEMCITABINE-PRETREATED PATIENTS WITH ADVANCED/METASTATIC PANCREATIC CANCER

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Purpose: To evaluate the efficacy and tolerance of the docetaxel/gefitinib combination as second-line treatment in patients with advanced pancreatic cancer. Patients and methods: A total of 27 patients pretreated with gemcitabine-based chemotherapy were enrolled onto the study. Docetaxel (75 mg/m^2, iv) was administered every 3 weeks for a maximum of 6 cycles and gefitinib (250 mg/d, p.o) continuously.

Results: One (3.7%) patient achieved a partial response (PR) and five (18.5%) patients stable disease (SD) [disease control rate (PR+SD): 22.2%, 95% CI: 6.5%-37.9%]. The median duration of the disease control, the median time to disease progression and the median survival were 3.1 (range 2–13), 2.3 (range 1–7.3) and 3.5 (range 1–13.9) months respectively. Grade 3/4 neutropenia was recorded in 10 (37%) patients, although only one (3.7%) developed grade 3 febrile neutropenia. One (3.7%) patient experienced grade 3 mucositis, one (3.7%) grade 3 fatigue and two (7.4%) grade 3 diarrhea. Grade 1–2 rash was observed in 13 (48%) patients. There were no treatment-related deaths. Conclusion: The docetaxel/gefitinib combination although safe has minimal activity as salvage treatment for advanced pancreatic cancer after failure of gemcitabine-based chemotherapy.

1083P PHASE I TRIAL OF CAPECITABINE (CAP) AND GEMCITABINE (GEM) WITH CONCURRENT RADICAL RADIOTHERAPY IN LOCALLY ADVANCED PANCREATIC CANCER (PAC): INITIAL RESULTS

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Background: Primary chemoradiation with infusional 5FU is widely used for the treatment of patients (pts) with locally advanced, unresectable PaC, but with disappointing results. Novel chemotherapy regimens in combination with radical radiotherapy (RT) thus need to be evaluated to improve the efficacy and pt convenience. The combination of Cap (Xeloda®) and Gem has shown superior activity in advanced PaC and both agents are potent radiosensitisers. The aim of this phase I trial was to determine the MTD of the Cap plus Gem combination with concurrent RT.

Patients and Methods: Eligible pts had unresectable, locally advanced PaC based on imaging and/or surgical staging, adequate organ function, ECOG PS 0-1 and no prior therapy. During RT, Gem was escalated from 20 to 50 mg/m^2/day IV (given days 1 and 4 of each week of RT), and Cap was escalated from 800 to 2000 mg/m^2/day (given daily in 2 divided doses, days 1-5 of each week of RT) in 7 planned dose levels. RT consisted of 50.4 Gy/ 28 fractions/5.5 weeks using conformal techniques. Three pts were entered to each dose level and if 1 of 3 pts had a dose limiting toxicity(s) (DLTs) the cohort was expanded to 6 pts. DLTs were defined prospectively and based on treatment-related toxicities and treatment interruptions.

Results: 16 pts have been accrued to date, with complete data on 14. Dose level 1: Cap/Gem; 800mg/m^2/day / 20mg/m^2/day (3 pts). Dose level 2: 1000 / 20 (8 pts). Dose level 3: 1300 / 30 (5 pts). Three pts (21%) had a PR, and 7 pts (50%) had SD. No DLTs were observed on dose levels 1 and 2, whilst 2 DLTs were observed in dose level 3; grade 3 dehydration (1 pt) and grade 3 diarrhoea and dehydration (1 pt). Dose level 2 was declared the recommended dose level and is being expanded to a total of 10 pts. No grade 4 haematological toxicities have been observed.

Conclusions: The addition of Cap and Gem to radical RT was both feasible and generally well tolerated. For future trials, Cap 1000 mg/m^2/day and Gem 20 mg/m^2/day (twice per week) is the recommended dose when combined with 50.4Gy of RT. Further results will be presented.

1084P ESTROGENE RECEPTOR EXPRESSION IN PATIENTS WITH CANCER OF THE STOMACH

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This study was aimed at the investigation of estrogen receptor expression (ERE) in patients with different forms of cancer of the stomach and estimation of a potential for antiestrogen adjuvant therapy in improving the results of the treatment. In 27 patients (10 females and 17 males) with cancer of the stomach, ERE was studied by using immunohistochemical investigation of micropreparations fixed with formaldehyde solution. Intensity of positive staining of estrogen receptors was estimated by using computer-aided imaging. Twelve patients had moderately differentiated cancer of the stomach, 3 patients - low differentiated, 7 patients - undifferentiated, and 5 patients had mucous cancer of the stomach. In all patients (except for 3 patients with G3), intense staining of estrogen-positive receptors was noticed in the nuclei of tumour cells, nuclei of lymphocytes, light zones of lymph follicles and nuclei of endothelium cells of the capillaries. In case of cancer of the stomach, estrogen-positive staining having optical density of 1.8 to 1.98 is spread over 12.4% to 74.7% of the nuclear zone of tumour cells. ERE in normal glandular cells of cervical zone was found in all patients. No correlation of the receptor status of a tumour with the patient's gender was noticed. Thus, tumour cells of moderately differentiated, low differentiated, undifferentiated and mucous cancer of the stomach are hormone-dependent, therefore, such cell may be susceptible to antiestrogen hormone therapy, e.g., with Toremifene, which makes it possible to expect an improvement of the results of the treatment. ERE (concentration) in non-tumour cells should be studied separately. This can be done by using quantitative imaging for immunohistochemical investigations.

1085P PACLITAXEL(PAXEL®)/5-FU/LEUCOVORIN (PFL) CHEMOTHERAPY IN INOPERABLE ADVANCED OR RECURRENT GASTRIC CANCER; A PRELIMINARY REPORT OF MULTICENTER PHASE II STUDY

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In patient with inoperable advanced or recurrent gastric cancer, a paclitaxel(Paxel®)/5-FU/leucovorin (PFL)combination chemotherapy was evaluated in a multicenter, open label, phase II setting. Paclitaxel(Paxel®) 75 mg/m^2 iv hr 0-2, 5-FU 2000 mg/m^2 iv hr 2-48 and Leucovorin 40 mg/m^2 iv hr 0-2 were administered every 14 days. 1 cycle of chemotherapy consisted of 2 chemotherapy sessions 14 days apart. Out of planned enrollment of 49 patients, 30 patients were enrolled from November 2004 to December 2005. Out of 30 enrolled patients, 3 patients withdrew and 27 cases were evaluable. A mean of 3.3 cycles of chemotherapy were administered. 12 patients (44.5%) showed partial response and 7 patients (25. 9%) showed stable disease with a disease control rate of 70.4%. Median survival time is not reached and mean survival time is 9.8 mos with a range of 3-15mo+. More than grade 3 toxicities of PFL chemotherapy were; nausea 1.2%, vomiting 1.8%, stomatitis 0.6% and anorexia 1.8%. There were no grade 3 or 4 hematologic toxicities associated with PFL regimen. Only 5.3% each of grade II anemia and leucopenia and 0.2% of neutropenia were noted. PFL chemotherapy appears very promising with ample efficacy devoid of severe toxicities.

1086P IRINOTECAN, LEUCOVORIN AND 5-FLUOROURACIL (ILF) VERSUS ILF PLUS CISPLATIN (PILF) FOR ADVANCED GASTRIC CANCER: INTERIM ANALYSIS FROM A RANDOMIZED PHASE II TRIAL

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Purpose: Irinotecan, in combination with 5-fluorouracil (FU) or cisplatin, clearly demonstrated efficacy against gastric cancer. We compared the combination of irinotecan, leucovorin and FU (ILF) with ILF plus cisplatin (PILF) as first-line chemotherapy in patients with measurable metastatic gastric cancer.

Methods: Patients with chemotherapy-naïve, histologically-confirmed, metastatic gastric adenocarcinoma were randomized to receive irinotecan 150 mg/m^2 on day 1, leucovorin 20 mg/m^2 and a 22-h infusion of FU 1000 mg/m^2 on day 1 and 2 (ILF), or ILF plus cisplatin 30 mg/m^2 on day 2 (PILF). Treatment was repeated every 2 weeks until disease progression, unacceptable toxicity, or patients' refusal. Primary endpoint was response rate, assessed every 4 cycles of chemotherapy.

Results: As of February 2006, 72 patients were enrolled and 56 were evaluable for efficacy. For both groups, 433 chemotherapy cycles were delivered (median, 5 for ILF and 6 for PILF). PILF was associated with, although statistically insignificant, substantially more grade 3 or 4 toxicities than ILF (44% and 38% of patients treated with PILF and ILF, respectively). However, no patient died of toxicity during treatment. Response rates were 39% and 48% (p=0.49) for ILF and PILF, respectively. Disease control (response plus stable disease) was achieved in 64% and 90% (p=0.02) of patients treated with ILF and PILF. Median progression-free survival (PFS) was 4.5 months (95% CI, 3.9-5.1) for ILF and 6.7 months (95% CI, 5.7-7.6) for PILF (p=0.01). For all patients, median survival time has not been reached yet but the estimated 1-year survival rate was 48%.

Conclusion: Both ILF and PILF combinations were active, with acceptable safety profiles. PILF appears to improve disease control and PFS, which merits further investigation.

1087P DETECTION OF EPSTEIN-BARR VIRUS BY IN SITU HYBRIDIZATION AND POLYMERASE CHAIN REACTION IN GASTRIC CARCINOMA

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Purpose: Epstein-Barr virus (EBV) has been known to be linked to a spectrum of neoplastic conditions, including nasopharyngeal carcinoma, Burkitt's lymphoma, peripheral T-cell lymphoma and Hodgkin's disease. This study aims to investigate the association of EBV with gastric carcinogenesis in Korea.

Methods: Fifty-three cases of gastric adenocarcinomas were studied for evidence of EBV infection by EBV-encoded small RNA (EBER) in situ hybridization (ISH) on the paraffin sections and amplifying the EBV genome encoding envelop glycoprotein (gp220) with polymerase chain reaction (PCR) in fresh gastric cancer specimens.

Results: EBER was detected in 7 (13.2%) of 53 gastric carcinomas and all EBER-positive cases were male. In 6 (85.7%) of 7 EBER-positive cases, the tumors were located in the upper and middle part of the stomach. EBER ISH study showed strong positivity in all the tumor cells, but negativity in surrouning lymphocytes, stromal cells and normal gastric mucosa in EBER-positive specimens. DNA PCR was positive in 23 (43.4%) of 53 gastric carcinoma, including all of 7 EBER-positive cases.

Conclusions: We could observe some association of EBV with gastric carcinoma and our findings concerning the distribution of EBV-positive gastric cancers by sex, site and histological type are similar to those in Japan. However, EBV-positive rate of gastric cancer is higher than that in Japan and lower than that in Western countries. Further studies should be performed to elucidate the oncogenic mechanisms of EBV in gastric cancer.

1088P DOCETAXEL (T) PLUS CISPLATIN (P) AND LEUCOVORIN/ 5FU (LF) IN 1ST LINE ADVANCED GASTRIC CANCER AND ADENOCARCINOMA OF THE ESOPHAGO-GASTRIC JUNCTION: RESULTS OF THE MULTICENTER PHASE II GASTRO-TAX-1 TRIAL

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Introduction: Studies combining T, P, and F every 3wks have shown superior efficacy but high rates of hematological toxicity in advanced gastric cancer. In order to reduce toxicity while maintaining the efficacy, we assessed an alternative schedule.

Methods: Chemo-naive patients (pts) with advanced esophago-gastric adenocarcinomas received T 50 mg/m^2, P 50 mg/m^2 day 1, 15, 29 and L 500 mg/m^2 plus F 2000 mg/m^2 d1,8,15,22,29,36 qd49. Because significant reductions to <80% of initial drug doses became necessary in 80% of pts, the regimen was amended after the first 15pts. Doses after amendment: T 40 mg/m^2, P 40 mg/m^2 day 1,15, 29 and L 200mg/m^2 plus 5-FU 2000 mg/m^2 d1,8,15,22,29,36 qd49. Primary endpoints were response and toxicity.

Results: From 03/04 to 08/05 we included 60pts: 42m, 18f; median age 53 yrs, (26-76); 24 adenocarcinomas of the esophagogastric junction, 36 gastric cancers. 24pts had locally advanced tumors and 36pts presented with metastatic disease. Pts received a median of 2 (range 0–4) cycles. Toxicity: reductions to <80% of initial drug doses were reported in 80% vs 60% of pts pre/post amendment. 2/60 (3.3%) pts died within 60 days after inclusion. Reported adverse events (grade 3/4) were: neutropenia 23.3%, febrile neutropenia 5%, diarrhoea 20%, nausea 8.3%, emesis 8.3% and fatigue 18.3%. 56 pts are evaluable for response: The overall response rate according to RECIST criteria is 50% (95%CI 37.6%–64.1%) including 2 CR. 42.9% had stable disease, 7.1% were progressive. Actual median follow up is 20.5mths with > 50% pts still alive. Mean survival is 17.3mths (95%CI 15.2–19.4). Median time to progression is 9.8mths (95%CI 5.6–14.0). Of the 24pts presenting with locally advanced tumors, 23pts underwent secondary resection. Tumor-free resection margins (R0) were achieved in 20/23pts (87%). Among 23 resected pts, major histopathological responses (<10% residual tumor cells) were seen in 9/23pts (39%).

Conclusions: The T-PLF regimen is highly active, safe and has an acceptable toxicity profile. In locally advanced disease, a high number of patients underwent potentially curative secondary resections.

1089P PHASE I/II STUDY OF COMBINATION CHEMOTHERAPY WITH S-1 AND CISPLATIN IN PATIENTS WITH PREVIOUSLY UNTREATED METASTATIC OR RECURRENT GASTRIC CANCER

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Introduction: S-1 plus cisplatin has been reported to be highly active in advanced gastric cancer (AGC). The objectives of this study were to define the maximal-tolerated dose (MTD) of S-1, given for 2 weeks separated by 1 week rest, with cisplatin, and to determine the activity and safety of this combination regimen at the recommended dose (RD) when used as the first line treatment of AGC.

Methods: Cisplatin was fixed at a dose of 60 mg/m^2 on D1 and the starting dose of S-1 was 30 mg/m^2 bid (level I) on D1 to D14 every 3 weeks. The dose of S-1 was increased by 5 mg/m^2 bid up to 50 mg/m^2 bid (level V) unless MTD was achieved. At every level, a cohort of 3 pts, which could be expanded to 6 pts, was studied. Dose-limiting toxicities (DLTs) were defined as usual manner and its occurrence was assessed for the first 2 cycles.

Results: From February 2004 to January 2006, 62 eligible pts were enrolled. In phase I (N=21), DLTs occurred at level V (S-1 50 mg/m^2 bid, N=3), with 2 of 3 pts developing G3 diarrhea or febrile neutropenia (FN). The RD was determined at level IV (45 mg/m^2 bid, N=6) because only 1 DLT occurred at this level. After the first 20 pts (series I) were enrolled in phase II, the protocol was amended; the S-1 dose was reduced down to 40 mg/m^2 bid (level III, series II, N=23) because of delayed hematologic recovery. At the time of analysis, a total of 236 cycles of chemotherapy were administered and 17 patients were still on protocol treatment in phase II portion. The median age was 56 years (range, 28-70) and ECOG PS was 0/1 in 98% of pts. The objective response was observed in 21(50%, 95% CI, 35-65) of 42 assessable pts. SD was achieved in 14 (33%) pts. With a median follow-up duration of 5.9 months, median progression-free survival was 5.6 months (95% CI, 4.6-6.6 months) and expected 1-year survival rate was 53%. G3 or worse toxicities included neutropenia (24%), anemia (21%), asthenia (14%), and diarrhea (9.5%); however G3 or worse febrile neutropenia, abdominal pain, and stomatitis were never observed.

Conclusion: New cisplatin plus S-1 regimen incorporating 2-weeks on and 1-week off is highly active against AGC with favorable toxicities profiles in Korean pts.

1090P EFFICACY AND FEASIBILITY OF PACLITAXEL AND CISPLATIN COMBINATION CHEMOTHERAPY FOR THE TREATMENT OF 5-FLUROURACIL (5-FU) REFRACTORY ADVANCED GASTRIC CANCER

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Background: Inspite many combination chemotherapy for advanced gastric cancer have been developed, only poor results have generally been reported. We performed a study on the combination chemotherapy of paclitaxel and cisplatin to the patients who have already treated 5-FU based chemotherapy. The primary objectives of the study were evaluating the disease response and elucidating the drug regimen's safety.

Methods: Patients who have treated 5-FU based chemotherapy (FAM, FA, FM, FP) with recurrent gastric cancer received intravenous paclitaxel 175 mg/m^2 on day 1, and cisplatin 75 mg/m^2 on day 2. This cycle was repeated every 3 weeks.

Results: From March 2000 to January 2005, 27 patients from were enrolled in this study. A total of 137 treatment cycles (median: 4 cycles) were administered. The responses were evaluable in 22 patients; 18 patients received this regimen as their 2nd-line treatment and the other patients received it as their third-line treatment. The objective response rate (RR) was 31.8% (95% CI: 12.8-40.3) with two complete responses, and stable disease was observed in 45.4% of the patients. The median follow up duration was 16 months for all the patients, and the median time to progression was 6.2 months (95% CI: 1.8-10.5). The overall survival time was 9.2 months (95% CI: 6.8-12.3) with a 1-year survival rate of 17.6% (95% CI: 5.2-32.6). The most common toxicity was neutropenia. WHO grade 3-4 neutropenia was occurred 7 patients (27%) and febrile neutropenia was observed in 4 patients (14%), grade 3-4 anemia and thrombocytopenia occurred in 2 patient (7.4%) and 3 patients (11%) respectively. Grade 3-4 non-hematologic toxicities included nausea in 6 patients (22%). There were no treatment related mortalities.

Conclusion: Paclitaxel and cisplatin produced promising activity against gastric cancer for the previously 5-FU treated patients as a 2nd-line treatment with an acceptable toxicity profile.

1091P MULTICENTER PHASE II STUDY OF WEEKLY PACLITAXEL PLUS CISPLATIN COMBINATION CHEMOTHERAPY IN PATIENTS WITH ADVANCED GASTRIC CANCER

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Background: Since weekly administration of paclitaxel has demonstrated sustained efficacy together with a more favorable toxicity profile (e.g. less myelotoxicity) than the 3-weekly administration, the present study was conducted to evaluate the efficacy and safety of a combination regimen of weekly paclitaxel plus cisplatin in patients with advanced gastric cancer.

Methods: Patients with previously untreated metastatic or recurrent, measurable gastric cancer received intravenous paclitaxel (Genexol®, CJ.Co. Seoul, Korea) 100 mg/m^2 plus cisplatin 35 mg/m^2 on days 1 and 8 in a 3-week cycle. Treatment was continued until disease progression, patient refusal, or anunacceptable toxicity up to 9 cycles.

Results: Fifty-two patients were enrolled in the current study. Of these, 46 were assessable for efficacy and 51 assessable for toxicity. Two complete responses and 17 partial responses were confirmed, giving an overall response rate of 36.5% (95% CI: 23.0% to 50.1%, intention-to-treat analysis). At a median follow-up of 193.5 days, the median time to progression was 6.8 months, whereas median overall survival was not reached yet. Grade 3 neutropenia occurred in 10 patients, while grade 4 neutropenia or febrile neutropenia was not observed. Most common non-hamatologic toxicity was nausea (grade 1/2 56.9%). There were no treatment-related deaths.

Conclusions: Weekly paclitaxel and cisplatin combination was found to be well-tolerated and effective in patients with advanced gastric cancer. Accordingly, this regimen can be regarded as an important first-line treatment option for advanced gastric cancer.

1092P PEMETREXED PLUS OXALIPLATIN IN THE MANAGEMENT OF ADVANCED GASTRIC CANCER: A MULTICENTER PHASE II TRIAL

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Introduction: Pemetrexed alone is active in patients with advanced gastric cancer. On the basis of different mechanisms of action of pemetrexed and oxaliplatin, and their potential synergistic interaction, we explored the combination in locally advanced/metastatic carcinoma of the stomach.

Patients and methods: The primary objective was response rate. Eligible patients had to ≥1 measurable lesion according to RECIST. Pemetrexed 500 mg/m^2 was given intravenously over 10 minutes, and oxaliplatin 120 mg/m^2 was given over 2 hours; both drugs were given on day 1 of a 21-day cycle. Patients were to receive ≥6 (maximum of 8) cycles unless disease progression occurred. Vitamin supplementation was given as well as dexamethasone. A total of 43 patients were planned in a two-stage design [alpha=0.05 (two-sided), power=80%]. An interim analysis was planned at the end of the first stage (13 patients), so the trial could be stopped if ≤3 responses were observed.

Results: Between May 2004 and October 2005, 44 patients (35 males and 9 females) entered the study. Median age was 63 years (range, 26-76). One patient (2.3%) had locally advanced disease, and 10 patients (22.7%) retained primary gastric cancer. Main disease sites included lymph nodes (54.5%) and liver (56.8%). A total of 216 cycles were administered (median 6; range, 1-8). All 44 patients were evaluable for efficacy with 5 complete and 10 partial responses (ORR 34.1%; 95% CI, 20.1%-48.1%). Stable disease occurred in 8 patients (18.2%). All the toxicities were manageable.

Conclusions: These preliminary data suggest that activity of the combination is promising in the palliation of gastric cancer. Final analysis of the study results will be available on June 2006 and will be presented at the meeting.

1093P IRINOTECAN/CAPECITABINE VERSUS CISPLATIN/CAPECITABINE IN ADVANCED ADENOCARCINOMA OF THE STOMACH OR GASTROESOPHAGEAL JUNCTION: INTERIMSANALYSIS OF A GERMAN AIO PHASE II STUDY

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Background: Irinotecan with 5-FU is highly effective in advanced gastric cancer. In addition, capecitabine seems to be as effective as 5-FU, with its advantage of oral administration. Thus, we compared efficacy and toxicity of irinotecan/capecitabine versus cisplatin/capecitabine in this prospective multicentric, open trail.

Methods: Patients (pts) with previously untreated locally advanced or metastatic adenocarcinoma of stomach or gastroesophageal junction and Karnofsky Performance status (KPS) of ≥ 60%, at least one measurable lesion and adequate organ functions were eligible. Pts were randomized to 3-weekly cycles of irinotecan 250 mg/m^2, day 1 (arm A) or cisplatin 80 mg/m^2, day 1 (arm B). Capecitabine was administered at a 1000 mg/m2 twice daily for 14 days followed by a 7-day rest in both arms. Primary endpoint was remission rate, treatment was continued until disease progression.

Results: At submission time, 91 of 120 pts (planned sample size) were randomized to arm A (45 pts) or B (46 pts). Interim data were available on 76 patients included into intent to treat analysis (34 pts arm A, 42 pts arm B). Baseline characteristics (arm A vs. B) were median age: 60 vs. 64 years, gender (female/male) 23%/77% vs. 30%/70%, KPS (≥80%) 97% vs. 93%, tumor distribution of gastric origin and gastroesophageal junction 85%/15% vs. 63%/37%. Grade 3 toxicities in A/B (% of pts) were anemia 3/9, neutropenia 17/19, diarrhoea 17/5, nausea 14/21, vomiting 3/14, hand-foot syndrome 6/2, respectively. Grade 4 toxicity occured only for neutropenia with 3% vs.5% in A/B, respectively. In 59 evaluable pts (28/31 in A/B), overall remission rate (CR + PR) and tumor control rate (CR + PR + SD) were 39% vs. 42% and 64% vs. 74%, respectively. Despite being only very descriptive, median progression-free and overall survival (arm A vs B) were 5.2 vs. 5.0 and 8.9 vs. 9.4 months, respectively.

Conclusions: In patients with advanced gastric and gastroesophageal cancer, both regimen irinotecan/capecitabine or cisplatin/capecitabine are effective, well tolerated and can be administered safely on an out-patient basis. Currently, both treatment arms are comparable.

1094P COMBINATION CHEMOTHERAPY OF S-1, DOCETAXEL AND CDDP FOR THE TREATMENT OF ADVANCED GASTRIC CANCER

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Purpose: A combination of 5-fluorouracil (5-FU), docetaxel and CDDP has been reported to be active for the treatment of advanced gastric cancer. However, severe toxicities of this combination have been pointed out. Recently, S-1, a new oral fluorinated pyrimidine compound consisting of tegafur, 5-chloro-2, 4-dihydroxypyridine and potassium oxonate, was proven to be significantly more effective and less toxic than 5-FU for advanced gastric cancer. In this study, we first performed a phase I/II study and subsequently phase II study of the combination of S-1, docetaxel and CDDP in patients with unresectable advanced gastric cancer.
Methods: Eligibility criteria were pathologically proven unresectable gastric cancer (stage IIIb - IV), PS 0 - 1, and no prior treatment. Doses of S-1 (80mg/m^2, d 1 - 14) and CDDP (60 mg/m^2, d 8) were fixed. Docetaxel (d 8) was dose-escalated from 60mg/m^2 (level 1) to 70 mg/m^2 (level 2), and then 80mg/m^2 (level 3). This treatment was repeated more than 3 times every 3 wks. Results: Twelve patients were enrolled. Toxicity and efficacy data of all the patients are available. At level 1 (n=4), no patient developed grade 3/4 toxicity. At level 2 (n=5), two patients developed grade 4 neutropenia, and one developed grade 3 nausea/vomiting. At level 3 (n=3), two patients developed grade 4 neutropenia and grade 3 nausea/vomiting. Dose limiting toxicities (DLT) were neutropenia and nausea/vomiting. Recommended dose (RD) was determined as docetaxel 60mg/m^2 (level 1). 91% of the patients achieved objective response consisting of 1 complete response and 10 partial responses, and only 1 patient showed disease stabilization. Four patients achieved down staging, and received subsequent gastrectomy. Of these, 3 have been disease free for more than 16 months, suggesting a possible complete cure. Median survival time was 476 days. On the basis of these data, currently phase II study is ongoing. Of the 16 patients assessable until today, 88% of the patients achieved objective response consisting of 1 complete response and 13 partial responses. One of the partial responders showed down staging and received curative gastrectomy.
Conclusion: Our regimen is feasible and shows a very high response rate with 15% curability.

1095P PHASE II STUDY OF CAPECITABINE AND CISPLATIN AS FIRST-LINE CHEMOTHERAPY IN PATIENTS WITH ADVANCED ESOPHAGEAL CANCER

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Background: 5-FU and cisplatin remains as standard treatment for metastatic esophageal cancer, producing response rates of 20 - 35%. Preclinical studies suggest synergistic anti-tumor activity of capecitabine and cisplatin.
Methods: This non-randomized open label phase II study was designed to evaluate the efficacy and safety of capecitabine 2500mg/m2/d on D1-14 and cisplatin 60mg/m2 on D1 every 3 weeks as 1st line chemotherapy in metastatic or recurrent esophageal cancer patients. Patients with; histologically proven, measurable lesions, age 18-75, ECOG PS 0-2, no prior chemotherapy in metastatic settings, life expectancy over 3 mo and signed written informed consent were eligible.
Results: Between Dec 2003 and Mar 2006, 45 patients were enrolled. The median age was 62 yo(47-72) and male:female ratio was 44:1. Nineteen patients had initial metastatic disease and 26 patients had recurrent disease. The most frequently involved metastatic site was lymph node(35). Of the 45 patients, 36 patients were assessable for treatment response. Three patients are receiving chemotherapy as of to date, 4 patients were lost to follow-up, and 2 patients had adverse events of tracheoesophageal fistula and tumor bleeding respectively. The overall response rate by intent-to-analysis was 57.1%(95% CI,42.7-71.6) with no CR and 24 PRs. SD was observed in 6 patients (14.3%) and 6 patients(14.3%) had PD. After a median follow-up duration of 15.8 mo(1.3-34.5 mo), median overall survival was 12.6 mo(95% CI,11.3-13.8) and median TTP was 4.4 mo(95% CI,3.0-5.8). A total of 176 chemotherapies were delivered and 163 cycles were evaluable for toxicities. Grade 3/4 hematologic toxicities included neutropenia(30), leukopenia(11), anemia(2), thrombocytopenia(1) and febrile neutropenia(2). Grade 3/4 non-hematologic toxicities included anorexia(16), fatigue(9), constipation(6), hand-foot syndrome(5), diarrhea(5), and stomatitis(3). There was no treatment related death.
Conclusion: The combination chemotherapy with capecitabine and cisplatin in advanced esophageal cancer demonstrated a promising anti-tumor activity and was well tolerated with convenient administration as a 1st line treatment.

1096P A PILOT STUDY OF TRASTUZUMAB MONOTHERAPY IN PATIENTS WHO PROGRESSED WHILE ON CHEMOTHERAPY FOR METASTATIC OR LOCALLY ADVANCED HER2-POSITIVE GASTRIC CANCER

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Background: Gastric cancer is the second most commonly diagnosed malignancy worldwide and remains one of the most frequent causes of cancer-related death. In many European countries it is often diagnosed at a late stage, thus leading to a poor prognosis. Currently, no standard regimen exists for the treatment of advanced gastric cancer. A prospective study has shown a significant association between HER2 overexpression and shorter disease-free and overall survival, suggesting that HER2 may be a promising target for therapy in gastric cancer. This study evaluates the efficacy and safety of trastuzumab (Herceptin®) monotherapy in patients with metastatic or locally advanced gastric cancer.
Methods: This is an ongoing multicentre pilot study in patients with HER2-positive gastric cancer (IHC 3+ or IHC 2+ / FISH+) who progressed under a previous platinum-based or 5-fluoropyrimidine-based chemotherapy. Patients received an initial loading dose of 4 mg/kg trastuzumab then weekly doses of 2 mg/kg. Efficacy end points include response rate (CR + PR) according to RECIST, duration of response, time to progression and survival rate.
Results: At the end of April 2006, 33 patients had been enrolled for testing by IHC and/or FISH. 14/33 patients were IHC 0, 11/33 were IHC 1+ and 5/33 were IHC 2+ / FISH-. Three patients were IHC 3+ and thus eligible for trastuzumab therapy. Due to sustained response (PR), one patient with IHC 3+ disease was treated for >24 weeks with trastuzumab monotherapy. After 24 weeks a slight progression was observed, so combination therapy with trastuzumab and carboplatin/5-fluorouracil/leucovorin was initiated, resulting in an additional PR after 18 weeks. The patient progressed again but achieved stable disease with a third experimental therapy: trastuzumab every 6 weeks in combination with daily erlotinib over 3 months.
Conclusion: Although the number of patients treated is still very limited, these preliminary results indicate that trastuzumab may be a therapeutic option in the treatment of HER2-positive gastric cancer. The study is ongoing and will be updated.

1097P PHASE I/II TRIAL WITH DOCETAXEL AND S-1 FOR PATIENTS WITH ADVANCED OR RECURRENT GASTRIC CANCER

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Background: S-1 and docetaxel (TXT) show significant single-agent efficacy in gastric cancer and are synergistic in vivo studies. We performed a phase I/II study of this combination chemotherapy to determine the maximum-tolerated dose (MTD), recommended dose (RD), and efficacy in unresectable or recurrent gastric cancer.
Methods: Docetaxel was administered intravenously on day 1 and S-1 was administered orally on days 1-14 every 3 weeks. Doses of each drug in the phase I study were as follows: TXT/S-1, level 1 60/60; level 2A 60/80; level 2B 75/60; level 3 75/80 (mg/m^2). Phase II study was being conducted with RD based on the phase I study.
Results: Total 56 patients (median age 54) were enrolled in this study (15 patients for phase I study, 6 for phase I study of elderly patients and 35 for phase II study). At level 3, 2 of 3 patients developed DLTs (grade 4 neutropenia with fever and grade 4 neutropenia with grade 3 stomatitis, respectively). Therefore, the dose at level 3 was determined as the MTD. Two patients (age 66 and 64 years old) developed fatal toxicity (grade 4 neutropenia with fever and shock) during the initial phase 2 study. Additional phase I study with level 2A for elderly patients over 60 years was conducted. No DLTs occurred at this level. So, level 2B for the younger patients and level 2A for the older patients were determined as the RD. A total of 295 cycles were administered (median 4, range 1-13). The most common grade 3/4 toxicities were neutropenia (41.1%), leucopenia (35.7%), and febrile neutropenia (26.8%). The response rate of the phase II study was 43.3% (95% CI: 0.26-0.61) and the disease control rate was 83.3% (95% CI: 0.70-0.97). The preliminary median survival time and time to progression were 345 (95% CI: 243-447) and 224 (95% CI: 153-295) days, respectively.
Conclusion: This combination regimen showed high disease control rate and was also well tolerated in patients with advanced gastric cancer.

1098P CHANGES FROM BASELINE HEALTH RELATED QUALITY OF LIFE (HRQOL) ANALYSIS: NO COMPROMISE BY ADDING DOCETAXEL TO A CISPLATIN-BASED REGIMEN IN ADVANCED GASTRIC CANCER PATIENTS, INCLUDING THOSE EXPERIENCING FEBRILE NEUTROPENIA (FN) OR NEUTROPENIC INFECTION (NI)

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Background: The docetaxel (Taxotere®, T), cisplatin (C) and 5-fluorouracil (F) regimen significantly prolonged median time to progression (TTP) (5.6 vs 3.7 months) and median overall survival (OS) (9.2 vs 8.6 months) compared with CF in the first-line treatment of advanced gastric cancer (GC) (Moiseyenko. J Clin Oncol 2005;23[Abs 4002]). The time to 5%, 10%, 20% and 30% definitive deterioration in HRQoL occurred significantly later with TCF compared with CF (Moiseyenko. Eur J Cancer 2005;3[Abs 205]).

Objective: To assess the impact of adding docetaxel to standard chemotherapy on HRQoL in the TAX 325 Phase III clinical trial using a change from baseline analysis.

Methods: HRQoL was assessed by the EORTC QLQ-C30 and EuroQoL EQ5D questionnaires at baseline, every 8 weeks from baseline, and every 3 months after progression. Analyses were performed on mean score changes between the two treatments from baseline for both instruments. We also investigated the impact of FN or NI events on HRQoL.

Results: In the 445 randomised patients, baseline compliance rates for evaluable questionnaires were 86.0% vs 89.7% for QLQ-C30 and 78.7% vs 92.8% for EQ5D for TCF and CF, respectively. At baseline, the mean scores were 54.8 vs 56.2 for Global Health Status (GHS) and 62.8 vs 66.2 for the Visual Analogue Scale (VAS) for TCF and CF, respectively. The QLQ-C30 GHS mean scores showed a constant improvement from baseline, with no statistically significant difference between the arms for GHS and for 5 specific dimensions (physical functioning, social functioning, appetite loss, pain, nausea/vomiting). With the EQ5D, the VAS and Utility Index changes were similar in the two arms, with a global improvement in TCF vs CF for the VAS. No impact on HRQoL was observed in patients experiencing FN or NI events vs those who did not experience them in terms of changes from baseline.

Conclusion: When added to CF, docetaxel significantly prolonged TTP and OS in advanced GC. This HRQoL change from baseline analysis shows that TCF does not compromise HRQoL when compared with CF, even in patients experiencing FN or NI.

1099P CAPECITABINE (X) AND ETOPOSIDE (E) FOR PATIENTS (PTS) WITH LOCALLY ADVANCED OR ADVANCED GASTRIC CANCER (AGC): A MEXICAN ONCOLOGY STUDY GROUP PHASE II TRIAL

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Background: Palliative chemotherapy is the mainstay of treatment for >60% of pts with non-resectable/AGC and for 80% of pts with recurrent disease after surgery. As toxicity of the most popular regimens remains high, more effective and better tolerated regimens are clearly needed. The oral fluoropyrimidine X (Xeloda®) has proven efficacy and safety in colorectal and breast cancer. Phase II data in AGC suggested that X can replace 5-FU with comparable efficacy and potential safety/convenience advantages. This phase II study evaluated the XE combination in poor-prognosis pts with AGC. Methods: Pts with previously untreated locally advanced non-resectable or recurrent AGC were treated with X 1000 mg/m^2 orally bid d1-14 + E 120 mg/m^2/d x3d, q3w. Primary objective was response rate (RECIST criteria); secondary aims were safety, quality of life (QoL), progression-free survival (PFS) and overall survival. Results: Baseline characteristics of the 65 pts enrolled were: male/female 54%/46%; median age 53 years (range 29-74); ECOG PS 0/1/2 (25%/58%/17%). Main metastatic sites were: stomach 66%, lymph nodes 21%, liver 9%, other 20%. Median number of delivered cycles was 5 (range 1-14). In the 53 evaluable pts, overall response rate was 38% (including 6 CRs and 14 PRs), with stable disease in 34% of pts. Treatment is ongoing in 12 pts and 1 pt died during treatment. At a median follow-up of 4.6 months (95% CI, 2.3-7.2), median PFS and median survival have not yet been reached. QoL improved in 9 of 15 domains of which the following were significant: global health status (p=0.045); fatigue (p=0.013); pain (p=0.033); loss of appetite (p=0.002); physical functioning (p=0.027); emotional functioning (p=0.004). The remaining scales showed no change or non-significant impairment (constipation). The most common grade 3/4 adverse event was neutropenia (14%); all other events occurred in <5% of pts. Conclusions: XE was well tolerated and QoL was improved or maintained. These findings are impressive given the poor prognosis of the pt population and suggest that this combination should be evaluated further.

1100P THE ROLE OF LYMPH NODES ON DISEASE FREE SURVIVAL IN OPERATED GASTRIC CANCER (TURKISH ONCOLOGY GROUP STUDY)

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Objectives: The standard treatment in early stages of gastric cancer is surgery with lymph node dissection. In this study, our aim was to determine the nodal factors that are effective on disease free survival (DFS) in gastric cancer.

Patients and Methods: A total of 372 patients (121 females, 33%; 251 males, 75%) with gastric cancer operated in various centers in Turkey were evaluated retrospectively. The mean age of the patients were 59+12years (19-85). Among the patients, 27.% did not have nodal metastasis, whereas 269 patients 73% had nodal metastasis. Median DFS was 81 months in the patients without nodal metastasis, whereas it was 19 months in those with nodal metastasis (p.00001). The mean number of lymph nodes dissected during the operation was 20.7+12.8 nodes (2-61). In 55.4% of the patients, the dissected lymh node number was over 15. There was no correlation between the number of dissected lymph nodes and DFS. Among the patients who had lymph node metastasis, the mean lymph node diameter was 1.73+.8cm. among the patients with nodal metastasis, 41,1% had N1, 20.4% had N2, 10.8% had N3 disease. Median DFS in N1 patients was 21months, whereas it was 14 months in N2 patients and 9 months in N3 patients (p.01, p.00001, p.0014, respectively). Immune-reactive lymph nodes (NR)were determined among the dissected nodes and were ranked according to their numbers as NR0, NR1 (1-6 reactive nodes), NR2 (7-15 nodes), NR3 (>15 positive nodes). Among NR0 patients, DFS was 7 months, whereas it was 17 and NR1 patients, 33 months in and NR2 patients, respectively (p.04, p03, p.0007). The patients were divided into 3 groups according to the number of the dissected nodes divided by number of positive nodes as A (<3), B (3-10), and C (>10). Median DFS was 12 months in group A, 21 months in group B, and 38 months in group C (p.03, and p.005).

Conclusion: Our study suggests that presence of lymph node metastasis, N status, number of immune-reactive lymph nodes, and the ratio of the dissected/affected lymph nodes were effective on the DFS in operated gastric cancer. The relationship of DFS with the number of immune-reactive lymph nodes seems to be a striking observation, which to our knowledge, has not been reported before.

1101P SALVAGE CHEMOTHERAPY WITH IRINOTECAN, 5-FLUOROURACIL AND LEUCOVORIN IN PATIENTS WITH ADVANCED GASTRIC CANCER

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Background: Although the role of 1st line chemotherapy has been well established in advanced gastric cancer (AGC), the role of salvage chemotherapy remains still not settled. Irinotecan is active as a single agent and not cross resistant to fluoropyrimidines and platinum in gastric cancer. So, we tried a combination of irinotecan with leucovorin (LV), and 5-FU continuous infusion (FOLFIRI) as a salvage chemotherapy in patients with AGC.

Patients and methods: Between Oct. 2003 and Apr. 2006, a total of 139 patients with AGC who had failed to fluoropyrimidine plus platinum and/or taxanes were treated in Asan Medical Center with following FOLFIRI regimen: Irinotecan (150 mg/m2 on day 1) as a 2-h infusion followed by LV 20 - 200 mg/m2, and bolus and infusional 5-FU 2.0 - 2.8 g/m2. Cycles were repeated every 2 weeks.

Results: Out of 139 patients, 74 (53.2%) had previous chemotherapy with all of fluoropyrimydine, taxane, and platinum; and 52 (37.4%) had previous exposure to two of the 3 agents. Of the 72 patients evaluable for response with measurable diseases, 1 (1.4%) achieved a complete response, and 9 (12.5%) partial responses, and 23 (31.9%) showed stable disease (disease control rate 45.8%; 95% confidence interval [CI], 34% - 57%). The median time to progression (TTP) was 2.6 months (95% CI, 1.6∼3.6 months) and the median overall survival was 6.5 months (95% CI, 5.6∼7.3 months). In 50 (45%) out of 110 patients in whom FOLFIRI chemotherapy was finished, TTP by FOLFIRI regimen was longer than that by previous chemotherapy. The treatment was well tolerated in general, but 2 patients died due to treatment-related neutropenic sepsis.

Conclusions: The response rate to FOLFIRI regimen was not so remarkable in previously treated patients with advanced gastric cancer, however, disease stabilization could be induced in a significant proportion of patients. The value of FOLFIRI regimen as a salvage chemotherapy should be explored further.

1102P CHEMORADIOTHERAPY IN THE ADJUVANT TREATMENT OF GASTRIC CANCER

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Purpose: To analyze the effect of surgery plus adjuvant chemoradiotherapy in patients with node positive adenocarcinoma of the stomach.

Patients and method: Ninety consecutive patients (25 female and 65 male) with a median age of 51 years (25-70) who underwent curative resection (D1 and D2) for gastric cancer, between January 2000 and December 2005 were included into trial. Patients with lymph node metastasis considered eligible for study. There were poor differentiated adenocarcinoma in 27 patients (30%) and intermediate differentiated in 63 patients (70%). T stage distributions were T1 in 3 patients (3,3%), T2 in 7 patients (7,7%) and T3 in 74 patients (82,3%) and T4 in 6 patients (6,7%). 37 patients (40.7%) underwent subtotal resection and 53 patients underwent total resection (59.3%). Median numbers of resected and involved lymph nodes were 17 (10-57) and 5 (0-29) respectively. The adjuvant treatment consisted of 400 mg/m2/d of 5-fluorouracil (5-FU), plus 20 mg/m2/d of leucovorin (LV), for five days, followed by 4500 cGy of radiation (RT) at 180 cGy per day, given five days per week for five weeks, with modified doses of 5-FU (375 mg/m2/d) and LV (20 mg/m2/d) on the first four and the last three days of RT. One month after the completion of RT, two five-day cycles of 5-FU (400 mg/m2/d) plus LV (20 mg/m2/d) were given every 4 weeks in order to complete 5 cycles.

Results: Median follow-up was 36 months. The most frequent tumour location was antrum (38%). Weight loss more than 10% was observed in 14 patients (15.5%). Grade II esophagitis emesis and leucopenia were 21%, 20% and 16%. Grade III diarrhea and leucopenia occurred in 2 (2.2%) and 3 patients (3.3%) respectively. Febrile neutropenia was not observed. During RT, grade IV local skin reaction occurred in 1 patient. Full course chemoradiotherapy was completed by 60% of patients. Loco-regional recurrence was observed in 3 patients (3.3%) and systemic recurrence was observed in 14 patients (15.5%). Most frequent systemic recurrence location was liver metastases in 5 patients (5.5%). Median survival was 36.2 months and overall survival rate was 48.6% for 3 years.

Conclusion: Concomitant chemoradiotherapy seems to be an effective and tolerable adjuvant regimen in curatively resected node positive stomach cancer

1103P SEQUENTIAL TREATMENT WITH CISPLATIN (P) IN COMBINATION WITH INFUSIONAL 5-FU/LV (PFL) FOLLOWED BY IRINOTECAN (Ir) + 5-FU/LV (IrFL) FOLLOWED BY DOCETAXEL (T) + 5-FU/LV (TFL) IN PATIENTS (PTS) WITH METASTATIC (M) GASTRIC CARCINOMA (GC): PRELIMINARY RESULTS OF A PHASE II TRIAL BY THE GRUPPO ONCOLOGICO NORD-OVEST (G.O.N.O.)

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Background: the combination of 5-FU and P is considered a standard treatment for MGC. Ir and T are active against GC and have an incomplete cross-resistance with P and 5-FU. The combination of Ir or T with P and 5-FU is feasible but with substantial toxicities. A different way to include Ir and T in the first-line treatment of MGC is to use them sequentially to a P/5-FU containing regimen.

Methods: we are conducting a phase II study in chemotherapy-naïve pts with measurable MGC according to RECIST criteria. Sequential treatment consisted of: 3 cycles of PFL (biweekly P 50 mg/sqm d1, LV 200 mg/sqm d1 and 5-FU 3200 mg/sqm 48-h c.i. starting on d1) followed by 3 cycles of IrFL (biweekly Ir 180 mg/sqm d1 and 5-FU/LV) followed by 3 cycles of TFL (biweekly T 50 mg/sqm d1 and 5-FU/LV). Evaluation of disease has been performed every 3 cycles.

Results: up today 37 pts have been enrolled: age (median/range)=58/34-71 years, sex (M/F)=29/8, sites of disease (single/multiple)=7/30, ECOG PS (0/1)=24/13. Main observed toxicities per cycle were (PFL/IrFL/TFL): grade 3 diarrhoea 1%/1%/0%, grade 3 stomatitis 0%/2%/3%, grade 3/4 neutropenia 3%/3%/9%. Nor febrile neutropenia neither toxic deaths have occurred. Among the 29 pts evaluable for response we observed 1 CR and 6 PR with PFL (RR 26%); responses improved in 9 pts with IrFL while 3 pts progressed; responses further improved in 5 pts with TFL while 2 pts progressed. Number of cycles administered per patient (median/range)=9/2-9. Response rate after the 9 planned cycles was 48% (4 CR, 10 PR). At a median follow-up of 9.0 mos median TTP is 7.0 mos and median OS is 13.4 mos. Conclusions: this sequential treatment is feasible with a favourable safety profile. Preliminary results in terms of activity and efficacy are promising.

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1104P PHASE I/II- STUDY WITH 5-FU, LEUCOVORIN, OXALIPLATIN (FLO) AND MITOMYCIN C (MMC; FLOM) IN PATIENTS (PTS) WITH PREVIOUSLY TREATED ADVANCED GASTRIC CANCER (AGC)

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Background: Median survival in pts with AGC rarely exceeds 10 months. With the use of second- and third-line therapies, quality of life and survival may be improved. FLO is an active regimen against AGC, and has a favorable toxicity profile (Al-Batran et al. *J Clin Oncol* 2004). MMC belongs to the most active single agents in the treatment of AGC. This study was conducted to evaluate toxicity, maximum tolerable dose (MTD) and efficacy of adding MMC to FLO in pts with pretreated AGC.

Patients and methods: A traditional 3-pts cohort escalating dose (MMC) study design was used. Pts received FLO: oxaliplatin 85 mg/m2 (2h), 5-FU 2600 mg/m2 (24h), leucovorin 200 mg/m2 (2h), d1, 15, and 29 plus MMC (6-12mg/m2) d1. Cycles were repeated every 6 weeks.

Results: 20 pts (median age, 63; median number of pre-treatment, 2, range 1-7) were enrolled in 4 treatment cohorts. All pts were evaluable for safety and 15/20 pts for efficacy; 3 pts are still on study. Median treatment duration was 2.7 months. The treatment was well tolerated with NCI-CTC grade 3/4 non-hematological toxicity (related) affecting less than 5% of pts. Main grade 3/4 toxicities were anaemia (4/20), neutropenia (6/20), thrombocytopenia (4/20), renal (1/20) and allergic reaction (1/20). Main grade 1/2 toxicities were anemia (8/20), thrombocytopenia (7/20), renal (7/20), leukopenia (5/20), nausea (7/20), senso-neuropathy (5/20), and hand-foot syndrome (3/20). Dose limiting toxicity occurred in 1 pt in the 12mg-cohort. Prolonged thrombocytopenia requiring treatment discontinuation or delay ≥2 weeks was observed in 8/20 pts. Therefore, although MTD has not been reached, no further dose escalation of MMC was performed. Objective responses were observed in 7 of 15 (47%) pts, 4 (27%) pts had stable disease and 4 (27%) pts progressive disease. Median TTP and median OS were 4 months and 6.8 months, respectively.

Conclusion: The recommended dose of MMC with FLO is 12mg/m2 every 6 weeks. FLOM is an effective and tolerable treatment option for previously treated pts with AGC. However, with this schedule, prolonged thrombocytopenia may represent a significant adverse event

1105P EARLY RESULTS OF A TRIAL OF TRASTUZUMAB, CISPLATIN, AND DOCETAXEL (TCD) FOR THE TREATMENT OF METASTATIC GASTRIC CANCER OVEREXPRESSING HER-2

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Background: Cisplatin and docetaxel are active agents in the treatment of metastatic gastric cancer. Our group and others have reported that 10-25% of gastric cancers overexpress HER-2, a potential target for therapy. We report on the first five patients enrolled in a multicentre single-arm phase II study undertaken to assess the activity of TCD therapy in patients with metastatic gastric cancer that overexpresses HER-2.

Methods: Patients had primary tumours of the stomach or GE junction, and were either FISH positive or 3+ positive on IHC for HER-2 overexpression. Patients were treated with cisplatin 75 mg/m2, docetaxel 75 mg/m2 and trastuzumab, all on day 1 of a 21 day cycle. The loading dose of trastuzumab was 8 mg/kg and subsequent doses were 6 mg/kg. Patients who developed cumulative toxicity to cisplatin or docetaxel could continue on trastuzumab as a single agent if progression-free.

Results: To date 55 patients have been screened and 9 (16%) had tumours positive for HER-2. Five patients have been enrolled, and four of these patients are currently receiving study therapy. A summary of the number of cycles received and best response is below. One patient (#3) died of an upper gastrointestinal bleed that was possibly related to study treatment and/or migrating stent. Other grade 3/4 toxicities include peripheral neuropathy, abdominal cramping, and neutropenia (1 patient each).

Patient Number	Number of Cycles Given	Best Response
1	11 (4 trastuzumab only)	CR
2	5	PR
3	5	PR
4	5	SD
5	10	PR

Conclusion: Though HER-2 positivity is not common in gastric cancer, rates in this study are consistent with previous reports. TCD appears to have promising activity in patients with HER-2 positive gastric cancer. Study accrual is ongoing and updated results will be presented at the meeting.

1106P RANDOMIZED PHASE II TRIAL OF NEOADJUVANT VS. ADJUVANT DOCETAXEL IN COMBINATION WITH CISPLATIN IN PATIENTS WITH LOCALLY ADVANCED GASTRIC CARCINOMA

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Purpose: The optimum treatment strategy for locally advanced gastric cancer (LAGC) has not been clearly established. To test the feasibility of neoadjuvant docetaxel combined with cisplatin (DC) in LAGC, we conducted a randomized phase II study comparing neoadjuvant with adjuvant DC chemotherapy in LAGC.
Patients and Methods: Patients with LAGC(stage IIIA-IV) were stratified by Japanese staging system and randomized to neoadjuvant vs. adjuvant DC chemotherapy. Patients randomized to adjuvant arm underwent surgery [D2 or higher] followed by 3 cycles of DC (docetaxel 36 mg/m2 + cisplatin 40 mg/m2 on D1, D8, q 3 wks). In neoadjuvant arm, patients received 3 cycles of DC followed by surgery.
Results: Eighty-eight (44 per arm) patients were enrolled in National Cancer Center in Korea. Among 42 evaluable patients in neoadjuvant arm, objective response to DC was documented in 27 patients [RR, 64.3% (95% CI, 49.8 to 78.8%)] with 1 CR and 26 PR's. There were 2 patients with PD (4.7%). Neoadjuvant arm tended to show down-staged pathologic findings (T0-2 43.6% vs. 34.2%, N0-1 53.8% vs. 36.8%) and higher R0 resection rate (81.4% vs. 72.7%) compared with adjuvant arm, but the differences were not statistically significant. There was no significant difference in DFS (median, 14.5 mo vs. 16.9 mo in the neoadjuvant and adjuvant arm, respectively) and OS (median, 32.6 mo vs. not reached in neoadjuvant and adjuvant arm, respectively) between these two arms, suggesting that the timing of DC chemotherapy may not significantly affect overall treatment outcome of LAGC. Neoadjuvant arm showed no major postoperative complications and a favorable toxicity profile with lower incidence of grade 3/4 toxicities than adjuvant arm; most common grade 3/4 toxicity was neutropenia, which occurred in 37.2% vs. 60.5% of patients in the neoadjuvant and adjuvant arm, respectively (P=0.036). Febrile neutropenia developed in one patient (2.6%) in the adjuvant arm only.
Conclusion: Neoadjuvant DC is a feasible approach to LAGC, with a high response rate and a favorable toxicity profile.

1107P GASTRIC CANCER: PREDICTORS OF RECURRENCE WHEN THE LYMPH NODE EXAMINATION IS INADEQUATE

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Background: The TNM classification (sixth edition) requires at least 15 lymph nodes to be examined to allow an accurate staging. However, in our environment, only 20% of patients have the recommended minimum of 15 nodes examined.
Purpose: To evaluate clinicopathological predictors of recurrence in patients with gastric cancer undergoing radical resection with an inadequate number of lymph nodes examined.
Methods: 101 patients were included in this retrospective cohort. We evaluated age, gender, tumoral location, Borrmann type, Lauren histotype, type of gastrectomy, grade, invasion depth of tumor, lymph node involvement, ratio between metastatic and total number of excised lymph nodes keeping 20% as the cutoff value (LNR) and adjuvant treatment. The association between these variables and recurrence was investigated by using univariate methods and multivariate logistic regression analysis.
Results: Median (range) age was 63 years (44-85). 63% males, 37% females. Median follow-up time for the whole patients population was 36 months (10-104). Median number of lymph nodes analysed was 6 (0-14). Recurrence: 50 of 101 cases (49,6%); 41 hematogeneus dissemination, 9 locoregional recurrences. The following factors were found to be correlated with the recurrence risk: tumoral location, invasion depth of tumor, lymph node involvement and LNR. A multivariate analysis revealed that depth of invasion [odds ratio (OR) 2.80, 95% confidence interval (CI) 1.03-7.58, P=0.04] and LNR (OR 2.34, 95% CI 1.05-5.21, P=0.03) were independent risk factors for recurrences of gastric cancer. Median time to recurrence: 16 months (2-50). 82% of recurrences occurred within the first two years after surgical treatment. The estimated cumulative risk of recurrence at five years: 61% in the whole patients population, with serosal invasion and LNR > and ≤ 20% was 82% and 44%, without serosal invasion 73% and 39% respectively.
Conclusions: Invasion depth of tumor and LNR were independent predictors of recurrence in gastric cancer after potentially curative resection with an inadequate number of lymph nodes examined.

1108P MATURE DATA ON CAPECITABINE (X) + FRACTIONATED CISPLATIN (P) AS FIRST-LINE THERAPY IN PATIENTS (PTS) WITH ADVANCED GASTRIC CARCINOMA (AGC)

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Background: Gastric cancer is one of the most common malignancies in Asia with an adjusted mortality rate above 25/100,000 population. 5-FU + fractionated P is a standard treatment for AGC in China. In a Korean study by Kim et al., X + P produced a response rate of 55% in pts with previously untreated AGC. Here we present mature efficacy/safety results in Chinese pts with AGC.
Methods: 154 pts of a planned population of 120 pts were enrolled between Jun 2002 and Aug 2004. All had measurable AGC (WHO), Karnofsky performance status ≥60, adequate bone marrow, renal and hepatic functions. Prior radiotherapy or adjuvant chemotherapy was permitted. Pts received X 1000mg/m2 orally bid on days 1-14 + P 20mg/m2/day i.v. on days 1-5, every 3 weeks for 6 cycles. The primary endpoint was time to disease progression (TTP).
Results: Baseline characteristics of the 141 evaluable pts (104 men, 37 women) are: median age 54 years (range 23-80), main sites of metastases: lymph nodes 45%, liver 40%, stomach 18%, other 21%. The overall response rate was 36%, including 13 complete responses and 38 partial responses. After a median follow-up period of 12 months, the median TTP is 9 months (95% CI, 9-12 months) and the median overall survival is 12 months (95% CI, 12-15 months). Median treatment duration was 6 cycles (range 3-6). The most common treatment-related clinical adverse events (all grades >5%) were: hand-foot syndrome (HFS) 23%, leukopenia 13%, and SGOT abnormality 12%. The most common grade 3 adverse events were SGPT abnormality 3%, HFS 2%, and anaemia 2%. There were no grade 4 adverse events. Most grade 3 adverse events improved or resolved after treatment or interruption except in 1 pt with anaemia who withdrew after 2 cycles.
Conclusions: X combined with fractionated P is highly active and very well tolerated as first-line treatment for AGC, with comparable results to 5-FU + P.

1109P RESULTS OF A PHASE II STUDY OF A WEEKLY CISPLATIN (CDDP), EPIRUBICIN (EPI), FLUOROURACIL (5FU) AND FOLINIC ACID (FA) REGIMEN WITH G-CSF IN GASTROESOPHAGEAL (GE) AND GASTRIC (G) CANCER

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To evaluate the activity (ORR and resectability rate) and the toxicity of a weekly polichemotherapy in advanced GE or G cancer patients (pts) we performed a phase II study on 29 consecutive pts. CDDP 40 mg/m2, 5FU 500 mg/m2, EPI 35 mg/m2, FA 250 mg/m2 were given weekly with prophylactic G-CSF given from day 2 to 5. Pts'characteristics were as follows: median age 64 (34-81), M/F 19/17; 17 G and 12 GE cancers histologically confirmed;12 had only locally advanced unresectable disease; 8 had either primary unresected and metastatic disease (liver 2,nodes 2, peritoneum 2, lung 2, retroperitoneum 1); 5 had only metastatic disease (peritoneum 3; retroperitoneum 1; lung 1); 4 pts had this therapy as adjuvant. A total of 338 cycles were given (median 13/pt); all pts were assessable for toxicity (WHO) and 19 for response (WHO). The ORR was 58%: 2 CR (10.5%); 9 PR (47.4%). 3 pts had SD (15.8%) and 5 had PD (26.3%). Median duration of response was 9.4 months (mo) (95% CI 3.7-15). 17/19 pts (89%) experienced a clinical benefit (ORR + SD + symptoms relief). 7/12 initially unresectable pts were completely resected (resectability rate=58.3%); after surgery, 5 out of these 7 pts received this regimen as adjuvant treatment. G3/4 hematologic toxicities were: neutropenia 45%, thrombocytopenia 14%, anaemia 17%. Noteworthily 2 pts experienced a non life-threatening myelodisplastic syndrome. Nausea/vomiting (G3/4 10%) were the main non-hematologic toxicities. No treatment-related death was observed. A delay in the treatment administration occurred in 16 pts, while a dose reduction was required in 4 pts. The median survival (OS) was 10.3 mo (95% CI 3.7-16.8). 7 pts lived >15 mo. The median OS in the responders group was 12.6 mo (95% CI 9.4-15.7). In the resected pts the median OS was 14.2 mo (95% CI 10.2-18.3). Median time to progression was 7.3 mo (95% CI 5.3-10.1) in all evaluable pts and 11.9 mo (95% CI 8.7-15) in the resected group. Our findings showed this schedule to be highly active and feasible. The observed resectability rate suggests this regimen could be taken into consideration as neoadjuvant treatment in the design of future trials for locally advanced G and GE cancer pts.

1110P A PILOT TRIAL WITH A COMBINATION OF CAPECITABINE AND THALIDOMIDE IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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Based on the single-agent efficacies observed in phase II trials (Cancer 2004;101: 578-586 and Cancer 2005;103: 749-755), a pilot trial with a combination of oral capecitabine and thalidomide has been conducted in patients with unresectable, recurrent or metastatic hepatocellular carcinoma (HCC) to evaluate its efficacy and toxicity. The regimen consisted of capecitabine at a dose of 750 mg/m^2 po bid for 14 days every 3 weeks and thalidomide at 400 mg po bed time. Eligibility criteria included histological diagnosis of HCC, measurable disease, no prior systemic therapy, age ≥18 years, ECOG performance score (PS) ≤2, adequate hematological, hepatic and gastrointestinal functions, no metabolic encephalopathy, and informed consent. A total of 29 patients have been accrued. Two patients had never received the protocol therapy due to rapid deterioration of clinical condition after registration. Twenty-seven patients have been treated according to the protocol. Patient characteristics included median (range) age, 60 (48-77) years; male, 24; median ECOG PS, 1; cirrhosis, 22; hepatitis C antibody, 19; hepatitis B surface antigen, 4; hemochromatosis, 1; extrahepatic metastasis, 5. Eight patients were not evaluable for response since they received less than 2 cycles of protocol therapy. Five patients had grade 3 but asymptomatic, transient hyperbilirubinemia. Three patients had grade 1 hand-foot syndrome. Three patients had excessive somnolence which required a reduction of thalidomide dose to 200 mg. Among 19 patients evaluable for response (received ≥ 3 cycles of capecitabine), 1 patient had complete response for 5 months (Time to progression [TTP], 7 months), 4 had partial responses (TTP, 2.5, 5.0, 6.0, and 7.0 months) and 4 had stable diseases for ≥ 3 months. This experience suggests a moderate but noticeable clinical efficacy of the combination of oral capecitabine and thalidomide, at given doses and schedules, with acceptable and tolerable safety profile in patients with HCC (Supported by a grant from Celgene Corporation).

1111P EFFICACY AND SAFETY STUDY OF EPIRUBICIN AND ETOPOSIDE COMBINATION CHEMOTHERAPY IN ADVANCED HEPATOCELLULAR CARCINOMA

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Background: There is no consensus on the treatment of advanced HCC (AHCC) and systemic treatments have offered marginal clinical benefits. Recently, etoposide and epirubicin combination chemotherapy (EE) was evaluated in patients with AHCC, which proved to be effective, with a response rate of 39% with a median overall-survival (OS) of 10 months (Bobbio-Pavallocini, et al. Eur J Cancer 1997). We analyzed the efficacy and safety of EE in AHCC.

Patients and Methods: Between Dec. 1999 and Oct. 2005, 75 pts with AHCC were treated with EE. Among them, 35 patients who fitted the pre-set eligibility criteria (pathologic confirmation or AFP > 400 ng/ml with typical dynamic liver imaging, no prior systemic chemotherapy, ECOG performance status 0-2, Child-Pugh class A/B, measurable disease based on RECIST, adequate liver, renal function, and bone marrow reserve) were enrolled on this retrospective study. The EE consisted of epirubicin 40 mg/m^2 on D1 and etoposide 120 mg/m^2 on D1, D3, and D5. Treatment was repeated every 4 weeks. HBV-associated liver disease were found 80% of pts and 74% of pts had prior history of transarterial chemoembolization (TACE) using cisplatin.

Results: A total of 102 chemotherapy cycles were administered with a median of 2 cycles per pt (range, 1-8). Two pts had a partial response and 9 patients had a stable disease with a tumor control rate of 32% (95% CI, 17-48). With a median follow-up duration of 6.4 months, the median progression-free survival (PFS) and OS were 2.1 months (95% CI, 1.8-2.4) and 6.4 months (95% CI, 4.4-8.5), respectively. There is a tendency of improved PFS in pts with HBsAg(-) and peritoneal seeding (P=0.06, P=0.054). The OS was significantly better in pts with HBsAg(-) and CLIP score 0-1 (P=0.024, P=0.033). The main toxicities were hematologic events including G3 or worse neutropenia in 28.6% and febrile neutropenia in 11.4% of pts.

Conclusion: The EE showed minimal anti-tumor activity with relatively tolerable toxicities in HBV-associated AHCC, especially in pts with prior history of TACE. Trials on newer chemotherapeutic agents are eagerly needed in the near future.

1112P PHASE II STUDY OF S-1 IN PATIENTS WITH UNRESECTABLE OR RECURRENT BILIARY TRACT CANCER (BTC)

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Background: S-1, an oral agent containing tegafur, gimeracil and oteracil potassium at a molar ratio 1: 0.4: 1, showed a response rate of 21% (n=19) for BTC in our pilot study. The objective of this study was to confirm the efficacy and feasibility of S-1 against BTC.

Methods: Eligibility criteria were unresectable or recurrent BTC with histological confirmation of adenosquamous or adeno carcinoma, at least one measurable lesion, Karnofsky performance status of 80 to 100%, age of 20 to 74 years, adequate organ functions, no prior chemotherapy, and written consent. S-1 was orally administered, 40 mg/m^2/dose b.i.d. for 28 consecutive days, repeated every 6 weeks, until disease progression or unacceptable toxicity.

Results: Forty-one patients were enrolled between January and December in 2004 with one patient excluded from analysis because of no treatment. The sites of primary tumors, gallbladder/ extrahepatic bile duct/ ampulla of Vater were 20/15/5. Twenty-two and 18 patients had unresectable and recurrent disease. Objective tumor responses were 14 partial response (9 gallbladder, 4 extrahepatic bile duct, 1 ampulla of Vater), 17 stable disease, 7 progressive disease and 2 patients were not evaluated, resulting in a response rate of 35% (95% c.i. 21-52). The median time to progression and survival time were 3.7 months (95% c.i. 3.2-5.8) and 9.4 months (95% c.i. 6.0-11.0). The main grade 3-4 toxicities were lymphopenia (18%), anemia (8%), and fatigue (8%). The incidences of other grade 3-4 toxicities were 5% or less.

Conclusions: Monotherapy with S-1 was active and feasible against BTC.

1113P PROGNOSTIC FACTORS FOR SURVIVAL IN INOPERABLE BILIARY TRACT CARCINOMA TREATED WITH GEMCITABINE AND CISPLATIN.

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Previously our group had reported the Phase II study result of gemcitabine and cisplatin as first-line chemotherapy in inoperable biliary tract carcinoma (Ann Oncology 2005:16:279-281). At that time we had 40 evaluable patients.After that period, we had treated another 70 patients with the same chemotherapy.We incorporated all cases together to assess the prognostic factors of these patient population.

Methods: From December 2000 to December 2005, 113 patients had received treatment with gemcitabine 1250 mg/m2 in a 30-min i.v.infusion on d1, 8 and cisplatin 75 mg/m2 in a 2-h infusion on d1 every 3 weeks.

Results: Of 113 patients enrolled ten patients were not evaluable due to incomplete treatment (7 patients were from 70 treated cases). One hundred and three patients were assessable for response and survival.There were 62 males and 41 females median age 51 years (range 30-69) median PS 1. One hundred cases were cholangiocarcinoma and three cases were gall bladder cancer. Median number of chemotherapy courses was four. Overall response rate was 33.0% partial response (PR in 34 pts) with 30.1% stable disease or minor response. Median survival time of the PR and SD patients was 14.8 months(range 2.8-23.5 mos.). Median survival time of all patients was 6.6 months (range 0.4-23.5 mos.). There were 4.0% grade 3 anemia 4.6% neutropenia and 1.8% thrombocytopenia there were 0.2%grade 4 anemia and 0.4% grade 4 neutropenia. Mild increase creatinine, skin rash, nausea, vomiting, neuropathy and myalgia were seen. Of all variable include age (under 60 vs over 60 yrs) performance status (0-1 vs 2), metastatic site (intraabdomen vs outside abdomen), serum albumin (less than 3.0 vs more than 3.0), baseline hemoglobin (less than 10 vs more than10), CA 19-9 (less than 200 vs more than 200), responders (PR plus SD vs PD) and surgery (hepatectomy vs none). Both univariate and multivariate analysis showed that only responders either PR or PR plus SD were significant for survival (p=0.046 for univariate and p = 0.044 for multivariate).

Conclusion: The most important prognostic factor for survival of inoperable biliary tract carcinoma was response to chemotherapy (both PR and SD).

1114P PHARMACOKINETIC (PK) AND CLINICAL PHASE II STUDY OF WEEKLY INTRAVENOUS KAHALALIDE F (KF) AS FIRST-LINE THERAPY IN PATIENTS (PTS) WITH HEPATOCARCINOMA (HC)

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Background: KF is a cyclic peptide isolated from an herbivorous marine mollusc, *Elysia rufescens*. In phase I studies, dose-limiting toxicity was liver toxicity and two patients with HC presented stable disease (for four and six months respectively).

Methods: This is a multicentre, open-label, non-randomized phase II study. The primary objective was to evaluate the efficacy of KF in patients with HC and the secondary objectives were to determine safety, tolerability and PK parameters. Therapy

consisted of KF 650 μg/m^2 over 1 hour every week until progression disease or unacceptable toxicity. Results: 22 pts were recruited, median age was 67 years (range 37-69) and ECOG PS was: 0=41%, 1=55%, 2=4%. Median sites of disease was 1 (range 1-2). All pts but one were chemonaïve. All pts were evaluable for toxicity and 21 were for efficacy. No objective response (RECIST criteria) was observed. Stable disease occurred in 9 patients (41%) with a median duration of 4.8 months (range 3.9-12.4). Median progression free survival was 2.4 months (95% confidence interval, 1.8 to 3.9 months). A >50% reduction in alpha-fetoprotein was observed in two patients. Grade 3-4 haematological toxicity was not observed, and grade 3-4 non-haematological toxicity included AST (46%), ALT (27%), GGT (64%), fatigue (5%) and hypersensitivity reactions (5%). PK: plasma clearance was higher than the calculated from the phase I program as a result of an increase of the volume of distribution (presence of ascites or other third spaces or a decreased albumin could explain this finding). Mean (SD) of half-life (hr), clearance (L/hr/m^2) and Volume of distribution at steady state (L/m^2) were 0.59 (0.26), 6.90 (2.93) and 5.97 (3.74) respectively.
Conclusion: Kahalalide F was well tolerated in this patient population, and stable disease was the best response observed in previously untreated patients with hepatocellular carcinoma.

1115P A PHASE II TRIAL OF TS-1 AND CISPLATIN IN PATIENTS WITH METASTATIC OR RELAPSED BILIARY TRACT CANCER(BTC)

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Background: Biliary tract cancers are still fatal and there is need of an efficient medical treatment. Systemic chemotherapy is increasingly being applied in advanced biliary tract cancer. We performed this study to evaluate the efficacy and toxicity of combination chemotherapy with TS-1 and cisplatin in metastatic or relapsed BTC as outpatient based regimen.
Methods: Eligibility criteria were pathologically-proven BTC with measurable tumor lesions, ECOG performance status (PS) 0 to 1, age 18 to 70 yrs, adequate hematological, renal and liver functions, no prior radiotherapy or chemotherapy, and written informed consent. The chemotherapy regimen consisted of TS-1 (40mg/m2 po bid from D1-14) and cisplatin (60 mg/m2 on D1), repeated every 3 weeks.
Results: Thirty-six BTC patients (metastatic: relapsed =26: 10, gallbladder: intrahepatic bile ducts: extrahepatic bile ducts =13: 20: 3) were enrolled from Jan. 2005 to Apr. 2006 and 26 of them were evaluable for response. Median age was 57 yrs (range, 37-70) and all patients had ECOG performance status (PS) of 0 or 1, except for 1 patient with PS 2. Median number of chemotherapy cycles given was 3 (range: 1-8). Out of 26 evaluable patients, complete response was observed in 1 patient (4%), partial responses in 9 (35%), stable diseases in 10 (39%), and progressive diseases in 6 (23%). Median time to progression was 19 weeks (95% C.I.: 10-28 weeks). Overall survival will be presented. Total 132 cycles were administered to the enrolled patients. Grade 3/4 anemia, neutropenia, and thrombocytopenia occurred in 7 cycles (5.3%), 9 cycles (6.8%), and 4 cycles (3%), respectively. Four events of grade 3 neutropenic fever (3%) occurred. Grade 3 nausea, vomiting, stomatitis, and diarrhea occurred in 3 cycles (2.3%), 2 cycles (1.5%), 2 cycles (1.5%), and 3 cycles (2.3%), respectively. Also, four events of grade 3/4 hyponatremia (including 1 event of grade 4) occurred.
Conclusion: Combination chemotherapy with TS-1 and cisplatin was relatively active and well tolerated outpatient based regimen in BTC patients.

1116P OUTCOME OF HEPATOBLASTOMA TREATED WITH THE JPLT (JAPANESE STUDY GROUP FOR PEDIATRIC LIVER TUMOR) PROTOCOL-2

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The Japanese Pediatric Liver Tumor Study Group has conducted cooperative studies to develop promising therapy for hepatoblastoma (HB) and hepatocellular caricinoma since 1991. In the first trial, JPLT-1, intraarterial administration of cisplatin/pirarubicin was studied in a total of 145 cases. The study provided 73.4% of 6-year overall survival (OS) and 66% of event-free survival (EFS), but failed to show any therapeutic advantage (J Pediatr Surg 37: 851-6, 2002). Poor prognosis of PRETEXT-IV or metastatic cases led us to launch JPLT-2 protocol, which investigates cisplatin/pirarubicin regimen (CITA), followed by second line of ifomide, etoposide, pirarubicin, and carboplatin (ITEC) for CITA non- responder, before and after curative resection of primary tumor and high dose chemotherapy with stem cell transplantation (SCT) for non-curative cases or metastatic tumors. From 1999 until 2005, 175 hepatoblastoma cases have been enrolled in the study, and 126 cases (76 male and 50 females) have completed the protocol including 23 cases (18%) with metastatic tumors. In the remaining cases, 7 were diagnosed as PRETEXT-I, 38 as II, 40 as III and 18 as Iv. The 3-year OS was 80% and EFS was 67%. The 3-year OS of the cases with PRETEXT, II or III tumors was 95%, while that of the cases with PRETEXT-IV or metastatic tumors was 54%. In 23 cases who underwent high dose regimen with SCT, only 13 cases (57%) were cured, indicating that high dose chemotherapy with SCT is not so effective in advanced tumors. With this regimen, 5 cases suffered treatment-related death. More promising strategies including liver transplantation and new targeting drugs should be developed for advanced hepatoblastoma.

1117P TRIPLET COMBINATION OF GEMCITABINE, OXALIPLATIN AND CONTINUOUS INFUSION OF 5 FU (''FOG'') IN THE TREATMENT OF LOCALLY ADVANCED OR METASTATIC CANCER OF GALL BLADDER.

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Introduction: There is an unusually high incidence of cancer of gall bladder (CAGB) in women in the northern part of Indian peninsula, with ASR ranging from 5.5 in Karachi (Pakistan) to 8.9 in Delhi and 8.1 in Kolkata (India). Most of these patients present in advanced stage in poor PS where curative surgery is not possible. At present, there is no accepted standard chemotherapy regimen. The most active agents are 5 FU, the platins and Gemcitabine. Doublet combinations give a response rate between 30 - 50% and overall survival of 8 - 12 months.
Aim: To test the safety and efficacy of a triplet combination of fixed doses of Gemcitabine 2000 mg on D1 and D8; Oxaliplatin 100 mg on D1 and D8, and 5FU 200 mg/day continuous infusion, the ''FOG'' regimen, in locally advanced or metastatic CAGB.
Results: This is a retrospective study. 69 patients - 59 females and 10 males, with median age of 53 years (range 21-73 yrs) were treated between 2003 - 2005. The response rate after an average of 4 cycles (range 1- 10) was 49% (8 CR and 26 PR) with SD in 12 cases and PD in 23. 4/8 CRs underwent surgery, 2 are planned for surgery, and one received radiotherapy. The median overall survival was 10 months. Non-neutropenic fever (possibly cholangitis) was recorded in 10 and mucositis in 5. Two patients died of septicemia while on treatment, one with neutropenia.
Conclusion: The triplet combination regimen ''FOG'' is well tolerated and appears to have a good response rate, with the ability to downstage the disease for potentially curative surgery. However, the survival rate remains poor and may reflect the advanced disease stage at presentation. A randomised trial comparing this with the doublet of Gemcitabine and cisplatin is planned.

1118P PEFG (CISPLATIN, EPIRUBICIN, 5-FLUOROURACIL,GEMCITABINE) REGIMEN IN ADVANCED BILIARY TRACT ADENOCARCINOMA (BTA)

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Background: BTA is an uncommon tumor with a poor prognosis and median survival time rarely exceeding 6 months. While most BTA is unresectable at diagnosis, there is currently no standard systemic chemotherapy. PEFG (cisplatin, epirubicin, 5-fluorouracil, gemcitabine) regimen is an effective upfront treatment in advanced pancreatic cancer (Reni M., J Clin Oncol 2001; Lancet Oncology 2005). This study assessed activity and safety of this combination regimen in patients with locally advanced or metastatic BTA.
Material and methods: PEFG (cisplatin and epirubicin 40 mg/m2 day 1, gemcitabine 600 mg/m2 day 1 and 8, 5-fluorouracil (FU) 200 mg/m2/day continuous infusion) was administered to chemotherapy-naive patients with locally advanced and/or metastatic biliary tract adenocarcinoma, citologically or histologically confirmed, ≤ 75 years, performance status (PS) > 60, adeguate organ function, till progressive disease or for a maximum of 6 months. Tumor was assessed every 2 months.
Results: Between May '99 and December '05, 37 (23 or 62% metastatic disease) patients, median age 62 (range 30-74), median PS 90, M:F=20:17, were treated with PEFG regimen at our institution. 13 (35%) patients had prior radical surgery. Primary tumor sites were intrahepatic bile ducts in 10 (27%) patients, extrahepatic bile ducts in 8 (22%), gallbladder in 12 (32%) and ampulla of Vater in 7 (19%). Chemotherapy is ongoing in 2 patients and 2 patients are not assessable for response due to clinical progression. Partial response and stable disease was observed in 16 of 37 (43%) patients and in 12 (32%), respectively. Median and 1-yr survival (OS) was 11.8+ months and 52%. Median and 6-months progression free survival (PFS) was 7.1+ months and 64%. 183 courses (range 1-8, median 6) of PEFG were delivered. Main grade 3-4 toxicity was: neutropenia in 17% of cycles followed by thrombocytopenia in 9%, nausea/vomiting in 4%, febrile neutropenia, anaemia and stomatitis in 2%, hepatic, diarrhoea and pulmonary oedema in 1%. A patient had a fatal cardiac infarction.

Conclusions: PEFG regimen demonstred to be active with a manageable profile of toxicity for patients with advanced BTA

1119P A NOVEL TRI-MODALITY TREATMENT OF STAGE II-III CARCINOMA OF THE ESOPHAGUS: INDUCTION DOCETAXEL/CARBOPLATIN, A DOSE-RANGING STUDY OF ORAL CAPECITABINE/WEEKLY DOCETAXEL AND THORACIC RADIATION FOLLOWED BY SURGICAL RESECTION

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Background: We previously reported our tri-modality approach in locally advanced esophageal carcinoma of induction docetaxel/carboplatin, wkly docetaxel, 5-fluorouracil (5-FU), thoracic radiation (RT) followed by surgery. This trial was designed with the same tri-modality structure while incorporating a dose-ranging study of oral capecitabine to increase the 5-FU exposure.

Methods: Thirty (30) patients (pts) with esophageal cancer were enrolled. Pts staged by CT, PET and endoscopic ultrasound (EUS). Induction therapy of docetaxel 80 mg/m2 and carboplatin AUC = 6 was given every 3 wks for 2 cycles. Thoracic RT (50.4 Gy in 28 fractions) with 5 wkly doses of docetaxel (15 mg/m2) and escalating doses of capecitabine (500 mg to 3000 mg) were given prior to each fraction of RT. Pts restaged by CT/EUS. If no evidence of disease progression, pts underwent a transhiatal esophagectomy 4-8 wks following the completion of chemoRT.

Results: Pt characteristics; 25 males, median age 64 (range 47-87), adenocarcinoma 27 pts, squamous cell 3 pts, EUS stage T3N0 = 3, T2N1 = 4, T3N1 = 22, T4N1 = 1, distal esophagus 12, GE junction 17, midesophagus 1. The MTD has not been reached at 3000 mg of capecitabine. DLTs of dysphagia (1 pt at 500 mg and 1 pt at 1500 mg), thrombocytopenia (1 pt at 2500 mg) and fatigue (1 pt at 3000 mg) have been noted. Five (5) pts experienced weight gain over the course of therapy and only 7 of 30 pts required a parenteral feeding tube. Median weight change was -3.3 kg (range of +5.5 kg to -18.7 kg). To date, the antitumor response by EUS was 70% (19 of 27 pts), 25 pts had R0 resection, 2 pts had pathologic complete responses. The median survival is 30.4 months with 68% and 52% alive at 1-yr and 2-yrs, respectively.

Conclusions: Overall survival is encouraging for this docetaxel and capecitabine based tri-modality treatment for bulky locally advanced esophageal cancer. Oral capecitabine at 3000 mg prior to each fraction of radiation is safe when administered in combination with 15 mg/m^2 of docetaxel and 50.4 Gy of thoracic RT. Funded in part by CA23108, Sanofi-Aventis, and Roche.

1120P CAPECITABINE (X) AND OXALIPLATIN (O) COMBINATION CHEMOTHERAPY IN PATIENTS (PTS) WITH ADVANCED GALL BLADDER OR BILIARY TRACT CANCER: A PHASE II STUDY

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Background: Advanced biliary tract carcinomas are associated with a very poor prognosis. This phase II study was conducted to determine the efficacy of X (Xeloda®) and O (Eloxatin®) combination chemotherapy in pts with inoperable gall bladder or biliary tract cancer.

Methods: Pts with inoperable locally advanced or metastatic adenocarcinoma of the gall bladder or biliary tract were eligible for this non-randomised, multicentre, open-label phase II study. Pts were treated with X (1000mg/m2 po, twice daily, days 1-14) and O (130mg/m2 i.v., day 1) every 3 weeks for up to 6 cycles. The primary objective was the objective response rate (ORR, RECIST criteria); secondary objectives were safety, progression-free survival (PFS) and overall survival (OS).

Results: 43 evaluable pts were recruited between July 2003 and January 2006. Baseline characteristics were: median age 61 years (range: 37-81); male/female (58%/42%); ECOG PS 0/1/2 (21%/64%/14%); primary tumour sites were bile duct (52%), gallbladder (43%) and ampulla of Vater (5%); 93% of pts had metastatic disease. 29 (67%) pts received 3 cycles and 11 (26%) pts received the full 6 cycles of chemotherapy. 10 pts were not evaluable for response. ORR (intention to treat) was 23% (95% CI, 12-39%), with 1 CR and 9 PRs. A further 13 pts (30%) had stable disease. Median PFS (all pts) was 4.9 months (95% CI, 3.2-6.5) and median OS (all pts) was 7.7 months (95% CI, 4.8-10.7). Grade 4 toxicity included nausea (2%) and vomiting (2%); grade 3 toxicity included fatigue (14%), diarrhoea (9%), vomiting (9%), nausea (7%), neuropathy (12%) and anorexia (2%).

Conclusions: This regimen was well tolerated in these pts, and has modest activity.

1121P CHARACTERIZATION AND TREATMENT OF 1200 PATIENTS WITH UNRESECTABLE HEPATOCELLULAR CARCINOMA (HCC): A 17 YEAR PROSPECTIVE EXPERIENCE

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Background: HCC is usually unresectable at presentation in the US. We have systematically followed 1200 biopsy-proven HCC patients (pts) over 17 yrs and now present initial database evaluation of pt presentation and results from 3 treatments: none (n=221), TACE (n=783) or Yttrium-90 (n=110).

Results: Descriptive-male:female=4:1. Median female survival=14 mo; median male survival=9 mo. Age ranges: 1-92 yrs, median 61 yrs. Cirrhosis 77% (median survival 7 mo vs 10 mo for absence). Hepatitis and survivals (median, mo): HBV 24%(14), HCV 37%(8), B+C 17%(8), none 21%(10). Alcohol, 5+ drinks/d 42% (8 mo vs 14 mo for none). Independent survival predictors were AFP (cutoff 25; median survival 25 vs 6 mo), bilirubin (cutoff 1.5; median survival 11 vs 3 mo), PVT (any=6 mo, none=15 mo), GGTP and Alk Phos. Tumor size 1-30, median 6.5 cm. Portal vein thrombus (PVT): main 17.7%, branch 45%. Survivals (mo) after therapy:

TACE or Y-90 or No Rx
AFP 25+: 7, 10, 2
AFP less than 25: 15, 18, 13
Bilirubin 1.5+: 5, 4, 2
Bilirubin less than 1.5: 11, 15, 10
Cirrhosis +: 8, 11, 3
Cirrhosis -: 10, 22, 3
Bilobar -: 10, 18, 4
Bilobar +: 8, 12, 1.5
Size 5cm or less: 10, 13, 10
Size 5+ cm: 9, 13, 2

Conclusions: Several subsets of HCC pts were found with distinct survival advantages.

1122P A PHASE II TRIAL OF WEEKLY IRINOTECAN AND CISPLATIN FOR CHEMOTHERAPY-NAÏVE PATIENTS WITH METASTATIC OR RECURRENT SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS

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Objective: This phase II study assessed the response rate and toxicity profile of weekly irinotecan and cisplatin combination for chemotherapy-naïve patients with metastatic or recurrent squamous cell carcinoma of the esophagus.

Patients and Methods: The eligibility criteria included histologically confirmed squamous cell carcinoma of the esophagus, no prior chemotherapy, adequate organ functions and written informed consent. Patients were treated with 65 mg/m2 irinotecan plus 30 mg/m2 cisplatin, both administered intravenously days 1 and 8, every three weeks.

Results: Between June 2003 and December 2005, a total of 29 patients were enrolled and all were assessed for response and toxicity. Ten patients achieved a partial response (34.5%; 95% confidence interval, 18.0 to 52.4%). With a median follow-up of 12 months, median progression-free survival and duration of response was 4.4 months and 5.3 months, respectively. The median survival time was 9.6 months with 1-year survival of 27.1%. Grade 3 or 4 neutropenia was observed in 48. 3% of patients and was the most common cause of dose reduction or therapy delay. However, non-hematologic toxicity was grade 3 asthenia (20.7%) and grade 3 diarrhea (13.8%) and grade 3 nausea/vomiting (3.4%) but there was no grade 4 toxicity.

Conclusion: This two-week on and one-week off schedule of weekly irinotecan and cisplatin combination has modest antitumor activity against squamous cell carcinoma of the esophagus, but has significant hematologic toxicity. However, the easy administration and favorable non-hematologic toxicity profile can make this regimen one of the standard treatments for squamous cell carcinoma of the esophagus.

1123P PROGNOSTIC FACTORS IN OESOPHAGEAL CANCER PATIENTS TREATED BY PREOPERATIVE CONCURRENT CHEMORADIOTHERAPY AND SURGERY

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Combined modality therapy in oesophageal cancer patients is suggested to prolong survival at the cost of higher toxicity. In this study we analyze various factors to establish prognostic factors for treatment outcome. 107 patients (pts), 93 men, 14 women, with operable oesophageal cancer were treated by neoadjuvant chemoradiotherapy (CRT) using CF regimen for 65 pts (61%) (carboplatin, AUC 6, IV on days 1 and 22, 5-fluorouracil, 300 mg/day, continuous infusion (CI) on days 1 to 42), or CPF regimen (CF plus paclitaxel 200 mg/m2/3hours IV on days 1 and 22) for 42 pts (39%) plus radiotherapy 45 Gy/25fr/5 weeks starting on day 1. Nutritional support was offered to all pts. Surgery was performed within 4-8 weeks after CRT if feasible. The influence of various clinical, laboratory, treatment and nutritional variables on survival was tested by univariate analysis with consecutive multivariate analysis of following factors: N-stage, performance status (PS), localization of stenosis, grade of dysphagia, relative pre-treatment weight loss, pathological complete response (pCR), pre-treatment serum levels of albumin, prealbumin, leptin, soluble leptin receptor (SLR) and tumour necrosis factor alpha (TNF-α). Median survival 20.0 months and 3-year survival of 32% was determined. Treatment with CF or CPF regimens did not differ significantly (p=0.512). Significant factors positively influencing survival in univariate analysis were: PS (0 vs. 1-2, p=0.012), grade of dysphagia (mild vs. serious, p=0.001), TNF-α level (lower vs. higher, p=0.028), pCR (yes vs. not, p=0.036). Other variables mentioned above were included to multivariate analysis due to trend in univariate one (p<0.2). Two independent factors influencing survival were found out in multivariate analysis: grade of dysphagia (mild vs. serious, p=0.017) and SLR (lower vs. higher, p=0.049). PS (0 vs. 1-2) had borderline significance of p=0.062.

Conclusions: Pre-treatment serum level of SLR and grade of dysphagia were found out to be independent survival prognostic factors in this study of multimodal treatment of oesophageal cancer. Values of leptin, SLR and TNF-α need further prospective follow-up.

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1124P MULTIVARIATE PROGNOSTIC FACTOR ANALYSIS IN PATIENTS WITH ESOPHAGEAL CANCER TREATED WITH PREOPERATIVE CHEMORADIATION: THE IMPORTANCE OF PATHOLOGIC RESPONSE AND LYMPH NODE METASTASIS

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Objectives: In the primary management of esophageal cancer, the rationale for chemoradiotherapy (CRT) followed by surgery is based on the pattern of both local and distant failure associated with surgery alone or CRT without surgery. The purpose of this study was to clarify which treatment-related variables could predict survival and recurrence in trimodality setting.

Patients and methods: Between January 1993 and March 2006, 183 patients were enrolled into two phase II and one phase III controlled tirals assessing neoadjuvant CRT at our institution. Among them, 133 patients (72.7%) underwent esophagectomy. We analyzed the prognostic factors of 105 patients who received curative surgery with adequate node dissection (>12).

Results: A pathologic CR was achieved by 45 patients (42.9%). Most patients (88.7%) are male and the median age was 63 years (range, 43 – 73). Operations performed included Ivor-Lewis (80.0%), transhiatal (7.6%) and McKweon(13%). With a median follow-up of 56.3 months, median OS of the entire group was 42.8 months (95% CI: 23.9 – 61.7), and the 5-year OS rate was 40.7%. Cancer-specific survival at 5 years was 55.9%. Median DFS was 32.2 months (95% CI: 21.1 – 43.3), and 5-year DFS rate was 36.1%. Dysphagia to solid food, weight loss more than 10% (< 6 Mo), non-responder, lymph node metastasis ≥ 2, recurrent laryngeal nerve involvement, or incomplete surgical resection were associated with poor survival in univariate analysis. In multivariate analysis, OS was better in responders after CRT and the patients who had ≤ 1 lymph node metastasis group (p=0.027, p=0.024, respectively). The survival of patients who had 1 positive node were similar to that of patients in the node negative group. DFS was better in the patients who had ≤ 1 lymph node metastasis group (p=0.02). Initial clinical stage was not a prognostic indicator of disease free or overall survival.

Conclusion: We suggest the number of LNs with metastasis is an independent prognostic factor in preoperative CRT setting. In addition, the non-responder after CRT was also associated with poor prognosis.

1125P COMBINATION CHEMOTHERAPY WITH GEMCITABINE AND CISPLATIN IN PATIENTS (PTS) WITH ADVANCED PANCREATIC CANCER

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Introduction: Gemcitabine is an active agent in advanced pancreatic carcinoma.The addition of cisplatin to gemcitabine has a synergistic tumoricidal effect, and may overcome the resistance to gemcitabine in some pts.The aim of this study was to investigate the efficacy and toxicity of this combination in pts with advanced pancreatic adenocarcinoma, including pts previously treated with gemcitabine.

Methods: Eligibility criteria included: locally advanced or metastatic adenocarcinoma of the pancreas with no or one prior chemotherapy, PS 0-2 and adequate bone marrow, hepatic and renal functions. The pts were treated with cisplatin 25 mg/m^2 and gemcitabine 1000 mg/m^2 on days 1, 8, and 15 of each 4-week cycle in the outpatient setting.

Results: sixty-six pts received this treatment.The median age was 61 years (y) (range 39–78y), median PS was 2 (range 0–2). Fifty-two pts (79%) had metastatic disease and 14 pts (21%) had locally advanced disease. Twenty-four pts (36%) received prior treatment with gemcitabine. Median number of cycles was 3 (range 1–16). The relative dose intensity was 0.72 for each drug alone and for the 2-drug combination. Grade III-IV hematological toxicity was thrombocytopenia in14 pts (21%), anemia in 9 pts (14%) and neutropenia in 5 pts (7%). Grade III-IV non-hematological toxicity was diarrhea and vomiting in only 2 pts each one. There was no drug-related death. Sixty-two pts were evaluable for response. Disease control (partial response and stable disease) was achieved in 33 pts (53%). There was no difference in disease control rate between gemcitabine-naïve and non-naïve pts. The median time to tumor progression (TTP) for the whole group was 2 months (m), (range 1-19 m) and the median overall survival was 5.5 m, (range 1-30 m). There was no difference in TTP between gemcitabine -naïve and non-naïve pts (3 m vs 2 m, respectively, p=NS), and no difference in survival (6.7 m vs 4.5 m, respectively, p=NS).

Conclusions: The combination of gemcitabine and cisplatin is active in advanced pancreatic carcinoma, even in previously gemcitabine-treated pts, with acceptable toxicity profile.

1126P GI-TAC: A RANDOMISED PHASE II STUDY OF SEQUENTIAL DOCETAXEL AND IRINOTECAN WITH 5-FLUOROURACIL/ FOLINIC ACID IN PATIENTS WITH METASTATIC UPPER ABDOMINAL (PANCREATIC-, GASTRIC- OR BILIARY) CANCER

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Introduction: The aim was to investigate the correlation to tumour marker changes and tumour activity among patients with upper GI cancer treated with sequential docetaxel and irinotecan together with 5FU and leucovorin. Secondary endpoints were survival, safety, symptom relief and quality of life.

Patients: During 2003–2005, 73 patient with metastatic upper GI-cancer were included, 22 gastric carcinoma, 28 pancreatic carcinoma and 23 with biliary carcinoma. The patients were randomised to receive either docetaxel 45 mg/m^2 or irinotecan 180 mg/m^2 every second week together with 5-FU/leucovorin (500 mg/m^2 + 60 mg/m^2 x 2, Nordic schedule, except patients with gastric carcinoma who were treated with the deGramont schedule). After every second course the patients were crossed over to the other arm. Treatment was given for six months.

Results: Despite of two treatment related deaths (3%), the treatment was well tolerated with totally 79 events of grade 3 toxicity and 10 events of grade 4 toxicity. The frequency of side effects were similar between the two treatment arms. 64 of 73 patients were eligible for an objective response. Response rates, time to progression and survival are shown in the table. All patients had symptomatic disease at inclusion, 29% had a subjective response, 52% had stabilisation of symptoms and 19% became worse after start of the treatment.

Results

Response/Tumour Type	Gastric	%	Pancreas	%	Biliary	%	Total	%
PR	7	35	6	24	4	21	17	27
SD	11	55	11	44	8	42	30	47
PD	2	10	8	32	7	37	17	27
TTP months (median)	4.9		5.5		2.8		4.4	
Survival months (median)	7.8		11.3		7.9		8.2	

Conclusion: Sequential treatment with docetaxel and irinotecan in advanced upper GI-cancer seems to be promising, especially among patients with pancreatic carcinoma. The results of the longitudinal tumour markers measurements will be presented.

1127P SECOND-LINE TREATMENT WITH PEMETREXED AFTER GEMCITABINE FAILURE IN PATIENTS WITH ADVANCED PANCREATIC CANCER: RESULTS OF A MULTICENTER PHASE II TRIAL

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Background: There is no established treatment regimen for advanced pancreatic cancer after failure of standard first-line chemotherapy with gemcitabine. Pemetrexed, a novel multi-targeted antifolate, has shown promising clinical activity in pancreatic cancer in previous phase II and phase III trials in the first-line setting.

Methods: This study was conducted to evaluate the efficacy and safety of pemetrexed in patients (pts) with unresectable locally advanced or metastatic pancreatic cancer (stage II-IV), ECOG performance status ≤2 and estimated life expectancy of ≥12 weeks (wks) after failure of first-line gemcitabine single-agent or combination therapy. Pemetrexed was started at 500 mg/m^2 q3w (10 min infusion) with vitamin B12 and folic acid supplementation. Dose escalation by 100 mg/m^2 every other cycle and an unlimited number of cycles were allowed. Primary endpoint was the 3-month survival rate. Here, we report the final follow-up results.

Results: A total of 192 treatment cycles (median 2, range 1–20) were given to 52 pts (60% male, median age 63 yrs, median time since initial diagnosis 32 wks, 89% stage IV disease). Doses were escalated in 2 pts (4%) and reduced due to toxicity in 9 pts (17%); the median dose per cycle was 500 mg/m^2 (range 212–700 mg/m^2). The 3-month survival rate was 75% (95% CI 63.2-86.8%). At a median follow-up of 20 wks (range 1-77), the median overall survival estimate was 20 wks, with 4 pts alive and 1 pt lost to follow-up. Median time to progressive disease was 7 wks (range 1–62). The overall response rate was 3.8% (0 CR, 2 PR); 12 pts (23%) had SD for ≥6 wks, 9 of them for ≥12 wks. CA 19-9 decreased at least once by ≥ 50% in 12 pts (23%). Grade 3/4 hematological toxicity rates per pt were as follows: neutropenia 17.3% (febrile neutopenia: 3.8%), leukopenia 15.4%, thrombopenia 5.8% and anemia 3.8%.

Conclusion: Pemetrexed is a feasible option for second-line therapy with mild toxicity and encouraging activity in unresectable locally advanced or metastatic pancreatic cancer after gemcitabine failure.

1128P DOSE-FINDING STUDY USING OXALIPLATIN (OX) IN COMBINATION WITH FIXED DOSE GEMCITABIN (GEM) AND RADIOTHERAPY (RT) IN PATIENTS WITH LOCALLY ADVANCED PANCREATIC OR BILIARY TRACT CANCER (PBCA)

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Background: Prognosis of inoperable PBCa is poor. Large randomized studies in pancreatic cancer showed a better survival in patients (pts) with locally advanced (LA) in comparison with metastatic disease. Data on radiochemotherapy are scarce in pts with LA disease. Therefore, we performed this multicenter, phase I study on the combination of radiotherapy and Gem/Ox. This regimen showed superior activity to Gem alone in pancreatic cancer1.

Methods: After signed informed consent, pts with LA pancreatic cancer (n=14) or biliary tract cancer (n=1) were included. They received two cycles of Gem/Ox followed by 5 weeks of RT (25 fractions of 1.8 Gy up to a total dose of 45 Gy) in combination with a weekly fixed dose of Gem (300 mg/m^2 in 30') and an escalating weekly dose of Ox (levels: 40/50/60 mg/m^2). NCI-CTC 2.0 was used weekly to score treatment-related toxicity in all pts.

Results: Today, 15 pts. with a median age of 61 y (range: 44-74), median Karnofsky performance score 90 (range: 70-100) and M/F=8/7 were included. Upto 60 mg/m^2 Ox, no disease limiting toxicity (DLT) occured. Grade 3 toxicity included nausea (n=1), neutropenia (n=3) and thrombocytopenia (n=1). This latter patient was treated with 40 mg/m^2 Ox and subsequently also experienced a grade 4. One patient receiving 50 mg/m^2 Ox developed a grade 4 thrombocytopenia. Most frequent grade 1/2 toxicity was nausea (n=8, 53%), thrombocytopenia (n=5, 33%) and diarrhea (n=5, 30%). Fourteen out of 15 received the full course of radiotherapy. Median time to progression (TTP) is 6.7 months (95% CI: 3.7-13.5). Thirteen out of 15 pts. are still alive.

Conclusions: Combination of radiotherapy and Gemcitabin/Oxaliplatin in pts with LA pancreaticobiliairy cancer is feasible and well-tolerated. The long TTP underlines the potential activity of this regimen. As no DLT has been reached, we will use a dose of 60 mg/m^2 Ox for further evaluation.

Reference

1. JCO 2005;23:3509–16.

1129P ERLOTINIB AS A SINGLE-AGENT THERAPY IN PATIENTS WITH ADVANCED PANCREATIC CANCER

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Introduction: Erlotinib (Tarceva ®) is an oral tyrosine kinase inhibitor of the epidermal growth factor receptor, recently shown to improve survival in advanced pancreatic cancer when given in combination with gemcitabine. There are no data related to its activity as monotherapy in this disease. We report our experience with erlotinib as a single agent therapy in patients (pts) with pancreatic cancer who have failed prior chemotherapy.

Methods: Eligible pts had advanced pancreatic cancer, progressing after one or more prior chemotherapy, ECOG PS 0-2 and adequate organ functions. Pts received erlotinib 150 mg/day until disease progression. Disease activity was determined by clinical evaluation, imaging and tumor markers.

Results: Ten pts were evaluable, M/F=5/5, median age 60 years (range, 49-84). Pts had locally advanced (LA) tumor (2 pts), abdominal spread (4 pts) and liver metastases (4 pts), and received a median of one prior line of chemotherapy (range, 1-5). Treatment duration was 1-12 + months (m). Grade II/III toxicities included rash (4/0 pts), acne (2/1 pts) and diarrhea (0/2 pts). In one pt dose was reduced to 75 mg/day. Median time to tumor progression was 1.5 m. However, 3 pts (1 LA, 2 liver) achieved clinical stabilization of disease with decrease in tumor markers (by 15, 30 and 75%) for 2 + m, 8+ m and 12+ m, and they are still on treatment.

Conclusions: erlotinib has antitumor activity as a single agent in pancreatic cancer. It can produce prolonged disease stabilization in pts progressing after chemotherapy.

1130P A RANDOMIZED PHASE II OF RADIATION AND CONTINUOUS INFUSION OF 5FU + DOCETAXEL OR DOCETAXEL + CISPLATIN IN THE TREATMENT OF LOCALLY ADVANCED PANCREATIC CARCINOMA. INTERIM ANALYSIS OF THE ACCORD 9 TRIAL

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Introduction: Locally advanced pancreatic carcinoma remains a challenging tumour with no clear standard of care in terms of radio-chemotherapy. The purposes of this randomized phase II trial was to determine the efficacy and toxicity of two experimental arms of radio-chemotherapy in histologically proven adenocarcinoma of the pancreas.

Methods: In arm A patients (pts) received docetaxel 20 mg/m^2 weekly and daily continuous infusion of 5FU at 200 mg/m^2 for six weeks, in arm B pts received docetaxel 20 mg/m^2 weekly and cisplatin 20 mg/m^2 weekly for six weeks. External beam radiotherapy: 54 Gy in 1.8 Gy fractions, six weeks. An interim analysis was planned after inclusion of 20 patients per arm: if the number of progression at 6 months was 13 or more in one arm, this arm should be stopped ; if not, 20 more pts are included.

Results: 40 pts (20 per arm) with disease considered to be unresectable but confined to pancreas and celiac nodes were included between 06/10/2003 and 01/08/2005. The arm A, but not the arm B, was stopped following the interim analysis. Only the results of arm A are reported here. 11 men, 9 women; mean age 61 years were included. Karnofsky index < 100: 14 pts. Location of the tumour: head: 14 pts, body: 5 pts, tail: 1pts. No information was obtained on chemotherapy in one patient, for the 19 others: 98% of the dose of 5FU and docetaxel was administered. The median dose of radiotherapy received by the patients was 54 Gy. Radiotherapy has to be interrupted in 3 pts. 9 pts experienced at least one episode of grade 3 or 4 toxicity. 6 had severe vomiting, 4 pts had severe nausea. No toxic death was observed. At 6 months, 18 pts had progressed. Median survival was 9.7 months. Median progression-free survival was 4.3 months.

Conclusion: The association docetaxel + FU + radiotherapy has very limited effect in patients with locally advanced pancreatic carcinoma. Doxetaxel based radio-chemotherapy is very well-tolerated. Inclusion in the arm docetaxel + cisplatin continues. Granted by Sanofi-Aventis

1131P THE EFFICACY OF FLUOROPYRIMIDINE-BASED SECOND LINE CHEMOTHERAPY IN ADVANCED AND METASTATIC PANCREATIC CANCER: RESULTS OF AN ONGOING ITALIAN/SWISS MULTICENTER SURVEY

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Background: Recent advances in the treatment of pancreatic cancer influence the management of locally advanced and metastatic disease. Nonetheless prognosis remains dismal and the impact on survival of palliative second-line therapy is hotly debated.

Methods: Clinical records of 160 Gemcitabine resistant/refractory pancreatic cancer patients (pts) treated in 11 medical oncology departments in Italy and Switzerland were reviewed. All pts received a fluoropyrimidine-based salvage regimen from June 1997 to February 2006. There were 99 males, 61 females, median age 62 years (range 34-78) and median ECOG performance status (PS): 1 (range 0-2). 16 different fluoropyrimidine-based salvage regimens were administered consisting of monotherapy in 59% of cases and platinum-containing doublets in 36%. Combinations with bevacizumab, irinotecan and mitomycin C were administered in the remaining 5%.

Results: Second line chemotherapy produced partial responses (PR) in 16 (10%) and stable disease (SD) in 40 pts (25%) by RECIST criteria. Overall tumor growth control (PR+SD) was 35%. The median progression free survival (PFS) was 2.65 months. Multivariate analysis revealed that the most important prognostic factor for PFS was PS, as pts with PS of 2 at the beginning of second line therapy had significantly worse results than those with PS = 0-1 (Second line PFS: 78 days vs 48 days, $p<0.05$). Baseline CA19-9 and number of metastatic sites were not independent prognostic factors for better second-line PFS. Pts who had responded (PR) to first-line Gemcitabine were more likely to respond or attain stable disease after second-line treatment, with a PFS of 2.6 vs 1.6 months ($p<0.05$). The overall survival (OS) for all evaluable pts was 11.5 months and 1-year survival was 45%. Within the limits of a retrospective study, OS appeared significantly improved by platinum-containing doublets (57 pts) with respect to other schedules (103 pts) with OS of 11.9 vs 10 months, $p=0.047$.

Conclusions: These results suggest that fluoropyrimidine-based salvage regimens have marginal activity and should be considered only in pts with a good PS who have responded to first line chemotherapy

1132P SALVAGE THERAPY IN ADVANCED PANCREATIC ADENOCARCINOMA

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Limited information on salvage treatment in patients with PA is available. At failure, over half of the patients are candidate for further treatment. A retrospective review of 154 patients submitted to salvage therapy at 3 Italian institutions has been performed to identify prognostic factors and provide useful information for patients counseling. Data on patient characteristics, diagnosis, treatment, progression and survival (OS) were collected. Inclusion criteria were: cytological or histologic diagnosis of PA and prior gemcitabine-including chemotherapy. Any age, performance status (PS) and chemotherapy regimen were considered. 154 patients (88 males; 142 metastatic; median age 60 years; median PS 80; 65 submitted to prior surgery, 27 submitted to prior radiotherapy) with a median previous progression-free survival (PFS) of 5.5 mo. (range 1-46 mo.) were included: 124 (81%) had received 1 prior chemotherapy line, 25 (16%) 2 lines, 5 (3%) 3 lines. Chemotherapy regimens were: cisplatin, epirubicin, 5fluorouracil (5FU), gemcitabine (PEFG; N=45); raltitrexed, oxaliplatin (TOM-OX; N=41), irinotecan-OX (N=30), mitomycin, docetaxel, irinotecan (MDI; N=15); docetaxel (N=10); 5FU plus either carboplatin or cisplatin (N=13). Median, 1yr and 2yr OS since first diagnosis were 16 months, 67% and 26%. Median and 6 mo. PFS since salvage therapy start were 2.8 mo. and 18%. Median, 1yr and 2yr OS since salvage therapy start were 5.8 mo., 13% and 3.5%. At univariate analyses, previous PFS and peritoneal disease significantly predicted OS while age, gender, PS, prior surgery, prior radiotherapy, number of previous chemotherapy lines, liver or pancreatic disease, number of metastatic sites, CA19.9 basal value did not. Multivariate analysis showed that previous PFS and PS predicted OS. Median and 1yr OS based on chemotherapy regimen was: PEFG 7.1 mo and 27%, MDI 6.1 mo and 0%; TOMOX 5.2 mo and 12%; 5FU-carboplatin or cisplatin 4.5 mo and 9%; irinotecan-OX 4.3 mo and 23%; docetaxel 3.9 mo and 0%. In both univariate and multivariate analysis PEFG regimen resulted more effective than other regimens. Irinotecan-OX had a borderline p-value ($p=0.06$) at multivariate analysis.

Salvage therapy appears worthwhile in patients with good PS and > 6 mo. PFS after upfront treatment.

1133P A DROP OF THE TUMOR MARKER CA 19-9 DURING CHEMOTHERAPY IN PATIENTS (PTS) WITH ADVANCED PANCREATIC CARCINOMA (APC) IS NOT A PREDICTIVE FACTOR FOR OVERALL SURVIVAL

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Background: The tumor marker CA 19-9 is elevated (>37 U/ml) in >80% of patients with APC. Several reports with limited patient numbers have linked a decrease of CA 19-9 during chemotherapy to prolonged survival. The aim of this study was to test whether this hypothesis holds true in a larger cohort of pts with prospectively collected CA 19-9 measurements.

Patients and methods: Serial serum measurements of CA 19-9 of all pts with histologically proven, locally advanced or metastatic carcinoma of the pancreas, treated in an international randomized study with gemcitabine monotherapy vs. gemcitabine/capecitabine combination therapy (SAKK trial 44/00 - Herrmann R et al. ASCO 2005, abst. 4010) were included in this analysis. Pts were excluded if serum CA 19-9 was below 1.0x upper limit of laboratory normal (ULN) or not measured.

Results: 247 out of 319 pts were evaluable for CA 19-9 analyses: 123 pts in the monotherapy arm, 124 pts in the combination treatment arm. Median overall survival for pts with a baseline CA 19-9 above the median value (i.e. 59x ULN, approx. 2183U/ml) was 5.8 months (mos) (95% CI 5.1-7 mos) and significantly shorter than for pts with baseline values below the median (10.3 months, 95% CI 8.6-12.8 mos, $p<0.001$). In a multivariate analysis, baseline CA 19-9 above the median was an independent negative prognostic factor for survival (HR 2.11, 95% CI 1.57-2.82, $p<0.001$).

CA 19-9 response to treatment was analyzed in 175 pts with baseline values >1.5x ULN: A drop of CA 19-9 during chemotherapy (baseline to first measurement after day 40) >25% corresponded to an increase in median time to progression (5.9mos, 95% CI 5.4-7.1 vs. 3.9mos, 95% CI 3.4-5.4, $p=0.002$), but not to a significant increase in median overall survival (10.3mos, 95% CI 9.3-12.1 vs 7.4 mos, 95% CI 5.3-10.3, $p=0.13$), neither did a drop of >35% ($p=0.21$) or of >45% ($p=0.22$).

Conclusion: Elevated pretreatment CA 19-9 is an independent adverse prognostic factor for survival, but a decrease during chemotherapy is not significantly associated with prolonged overall survival. Our data suggest, that a fall of CA 19-9 during chemotherapy is not a valid surrogate end point for survival in clinical trials.

1134P CA 19-9 CAN PREDICT EARLY RESPONSE IN PATIENTS (PTS) WITH ADVANCED PANCREATIC CANCER (PC)

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Background: PC is a fatal disease with a 5-years survival rate of less than 5%. The evolution of this disease is quickly fatal because at the time of diagnosis it is locally advanced or with distant metastasis and more than 90% of patients cannot undergo surgery and chemotherapy is used in this setting. The aim of this study is to evaluate if marker Ca 19-9 after 4 weeks of treatment is able to predict the early activity of chemotherapy.

Methods: PTS with metastatic and/or locally advanced disease were eligible for the study. Tumor response was assessed according to RECIST criteria with CT imaging every 3 cycles. Tumor markers (CEA, Ca 19-9), clinical benefit (including weight, performance status and pain assessment) and QoL was assessed weekly. All the PTS received first-line chemotherapy.

Results: Fifty-five PTS (median age 64,8 years, range 37,5-84; M/F=30/25) were enrolled; 21 PTS had locally advanced, whilst 32 had metastatic disease.

Eight PTS achieved a partial response (14.5%) and 20 (36.4%) showed a stable disease, whilst 27 (49.1%) PTS experienced progressive disease. Ca 19-9 measured at 4 weeks after the beginning of chemotherapy correlated with the activity of chemotherapy ($p=0.0044$).

Conclusion: Ca 19-9 can predict early response in PTS with advanced PC, representing an useful parameter in clinical practice.

1135 CAPECITABINE PLUS OXALIPLATIN (XELOX): CLINICAL EFFICACY AND SAFETY IN THE FIRST-LINE TREATMENT FOR METASTIC GASTRIC CANCER

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Background: Capecitabine is an oral fluoropyrimidine with proven efficacy and favourable safety in colorectal cancer, whose administration does not require hospitalisation or placement of central iv line. The trial was designed to evaluate the efficacy of XELOX in metastatic gastric cancer.
Patients and methods: To date 15 pts were enrolled in this study and treated with oxaliplatin 120 mg/m^2 on day 1 and capecitabine 1000 mg/m^2 twice daily from day 2 to day 15 every 3 weeks until disease progression or unacceptable toxicity. The evaluation of efficacy was performed every 3 cycles. The characteristics of enrolled patients were: M/F 9/6, Median age 57 yrs; median ECOG status 1 (range 0-2), all patients had adequate haematological, liver and renal function. The sites of disease were liver 8 pts, lymph nodes 6 pts, bone 1 pts and peritoneum 3 pts.
Results: All patients were evaluable for efficacy and toxicity. We registered 3 RC and 3 RP with an overall response rate of 40%, in 4 pts we registered stable disease, 5 patients progressed. 2 patients of 3 with RC had a single liver localization. The schedule was well tolerated, the main G 3/4 toxicity (according to NCI-CTC) observed were neutropenia 13% of the pts, diarrhoea 6% of the pts. Neuropathy G2 was recorded in 2 pts (13%). No treatment related death was reported.
Conclusion: The preliminary data of this study seems to show efficacy and good tolerability. These results are superior to those of historical controls from this institution, but it is necessary to confirm these data with a longer follow up and more patients.

1136 GASTRIC CANCER IN TURKEY:CHARACTERISTICS AND ETIOLOGY(A CASE CONTROL STUDY OF TURKISH ONCOLOGY GROUP)

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Gastric cancer is among the most common 5 cancer types in Turkey.In order to search the characteristics of gastic cancer patients and the role of diet and habits in the etiology, a case control study was undertaken by Turkish Oncology Group.Interviews of 254 patients diagnosed as gastric cancer in the year 2005 and healthy controls matched for each patient by age,sex and the geographic region they live were done by physicians.Median age of the patients was 58.5 ±12.7 years.Male:female ratio was 2:1.Illiteracy rate for the patients was 22.6%.Social Security covered 99.3% of the patients.Median time between the beginning of symptoms and the diagnosis was 3 ±10.1 months.Allmost 50% of the patients had received ampirical treatment before the diagnosis.Gastric cancer and any type of cancer in the families were present in 12.8% and 30.3% respectively.In 78% of the patients,the tumor location was distal stomach.Pathology was adeno cancer in 69% and signet ring cell cancer in 28.7%.Atrophic gastritis,H. Pylori and intestinal metaplasia were found in 27.3%,17.8% and 28.6% of the patients respectively. In the patient group,eating eggs,salted olives,and butter,drinking milk,smoking 2 packs or more cigarettes were significantly more common than controls.However,tooth brushing,antibiotic consumption, drinking coffee,eating meat,2-3 plates of vegetables a day,salad every day, tomatoes+cucumbers and bread in breakfast and fish in lunch/dinner were significantly more common in controls.Details of the study will bepresented at ESMO meeting in Istanbul.

1137 PHASE II STUDY OF DOCETAXEL, CISPLATIN AND MODULATED ORAL TEGAFUR (DCT) IN ADVANCED GASTRIC CANCER (AGC)

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Background: In a previous randomized trial, the combination of docetaxel, cisplatin and protracted venous fluorouracil (TPF) showed a high objective response rate (ORR) in AGC. Our cooperative group studied, in a previous fase II study, the combination of epirrubicin, cisplatin and modulated oral tegafur (EPT). The present study was planned to evaluate the efficacy and safety of a novel combination with docetaxel, cisplatin and modulated oral tegafur (TPT).
Methods: The main patient (pt) inclusion criteria have been a histologically demonstrated AGC, measurable disease, no prior chemotherapy except in adjuvant setting, and normal medullar, renal and hepatic functions. Candidates for radical treatment were excluded. The treatment schedule was Docetaxel (75 mg/m^2), Cisplatin (60 mg/m^2) day 1, oral Tegafur (500 mg/m^2) days 2-15, and oral continuous levofolinic acid (25 mg/d): one cycle lasts 3 weeks. Response was evaluated every 3 cycles. Dose adjustments were carried out according to the NCI Common Toxicity Criteria.
Results: 26pt were recruited. 26pt were assessable for toxicity and 24pt for efficacy. Median age was 65 years (39-76), male/female: 18/8. Metastases locations include: ganglionar (7pt), liver (12pt), peritoneal (9pt), pulmonary (3pt), other (6pt).
126 cycles were administrated (mean per pt: 4,84; with 15/26 received 6 cycles). No of dose reductions: 6/26.
Safety: Grade toxicities per pt were: neutropenia 5/26 (19%), asthenia 5/26 (19%), nausea/vomiting 2/26 (7%), stomatitis 2/26 (7%), anemia 2/26 (7%).
Efficacy: ORR was 54% (13/24 pt); 5pt showed complete response (21%) and 8pt partial response (33%). 8pt stabilised (33%) and 3pt showed progression (13%) during the treatment. Disease free survival was 8,2 months (3-15); overall survival was 10,3 months (5-25).
Conclusions: These results showed that TPT has a comparable activity profile to TPF, with reasonable toxicity. Oral protracted tegafur with levofolinate represents an alternative to protracted intravenous 5FU.

1138 RESULTS OF SURGICAL TREATMENT OF LOCAL SPREAD GASTRIC CANCER

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Methods: From 1998 to 2003, in 140 gastric cancer T4N2-3M0-1 patients, male 86 (61.4%), female 54 (38.6%) received extended-combined gastrectomy. The proximal stomach cancer, including transition to distal parts of esophagus had been diagnosed in 44 (31.4%) patients, in 32 (22.8%) patients cancer of stomach body and proximal parts and in 64 (45.7%) patients total stomach cancer. Infiltrative cancer growth was noted in 86 (61.4%) patients, endophytes in 34 (24.2%) and exzophytes in 20 (14.3%). All patients received extended-combined gastrectomy with D2 lymph dissection and resection 1 up to 4 adjacent organs. In 44 patients gastrectomy was performed with resection of distal part of esophagus. Total remote metastases were found in 11 (7.9%) patients; atypical liver resection was performed in 8 patients due to liver metastases. In 62 (44.3%) cancer invasion to the pancreas was diagnosed, in 26 patients distal pancreas resection, in 4 hemipancreatectomy, in 32 cases partial resection of pancreas. 62 patients are included in the control group; they received courses of systemic polychemotherapy, during 1995–98 years for local spread gastric cancer.
Results: Total postoperative complications it have been observed in 32 (22.8%) patients: in 4 patients-postoperative pneumonia, in 2 eventration, in 7 esophagoenterostomy leak, in 2 myocardial infarction, in 1 thromboembolism of pulmonary artery, in 4 pancreonecrosis, in 2 enteral fistula, in 2 hemorrhage and in 8 patients suppuration of postoperative wound. Postoperative mortality was 9.3% (at standard gastrectomy – 5.8%). One-year survival rate was 74.2±0.3%, 3 years were 28.2±0.4%, and 5 years were 7.5±0.4%. In the control group after chemotherapy the median survival was 8.2±0.4 months.
Conclusions: Invasion of tumor to adjacent structures or presence of remote metastases are not contra-indications for performance of operative treatment. The remote results of the extended-combined operation is better in comparison with polychemotherapy in control group and it gives the moral right to surgeons widely to perform the given kind of operation.

1139 CLINICAL PROFILE OF GASTRIC CANCER IN TURKEY: FACTORS EFFECTING DISEASE FREE SURVIVAL AND RELAPSE (TURKISH ONCOLOGY GROUP STUDY)

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Objectives: Gastric cancer is among the most common tumors in Turkey. In the early stages of gastric cancer the factors effective on disease free survival (DFS) and relapse of the disease need to be further elucidated.
Patients and methods: A total of 372 patients with gastric cancer who were operated in various centers in Turkey (121 females, 32.5%; 251 males 76.5%) were evaluated retrospectively. The mean age of the patients were 59.12 years (19-85). Among the patients 0.5% had Stage 0, 12.9% had Stage I, 18.5% had Stage II, 50.5% had Stage III, and 12.9% had Stage IV disease. The most common tumor localisazions were corpus

(48.9%), antrum (35.5%) and cardia (6.5%). Median DFS was 19 months in antrum tumors, whereas it was 7 months in cardia tumors (p.0018). Regarding tumor depth, 0.5% of the patients had T0 tumors, 6.2% had T1, 18.8% had T2, 68% had T3, and 4.8% had T4 tumors. Median DFS was 101 months in T1 patients, 36 months in T2 patients, 27 months in T3 patients, and 18 months in T4 patients (p.0003, p.0001, and p.0096). A negative surgical margin was provided in 86.3% of the patients. Median DFS was 26 months in magrin-negative tumors, while it was only 9 months in magrin-positive tumors (p.0049). Presence of lymphovascular invasion in tumor tissue was significantly related to lymph node metastasis (p.0028). The mean number of lymph nodes dissected at the operation was 20+12 nodes (2-61). 55.4% of the patients had more than 15 lymph nodes dissected. There was no relationship between the number of dissected lymph nodes and DFS. Among the patients 26% had N0, 41,1% had N1, 20.4% had N2, and 10.8% had N3 disease. Median DFS was 21 months in N1 patients, 14 months in N2 patients, and 9 months in N3 patients (p.01, p.00001, and p.0014, respectively). 36.2% of the patients had a relapse; 67.1% of the relapses were locoregional, whereas 32.9% were systemic relapses.

Conclusion: In Turkey, gastric cancer is seen twice as common in males and the most common sites are corpus and antrum. Tumor localisation, depth, surgical margin, and nodal involvement were factors that effect DFS. Our study suggests that the presence of lymphovascular invasion predicts the risk of nodal metastasis.

1140 GEMCITABINE PLUS OXALIPLATIN IN ADVANCED OR METASTATIC PRETREATED PANCREATIC CANCER

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Background: advanced pancreatic cancer has a very poor prognostic and gemcitabine remains most active treatment for this patients. There are some patients which are non-responders or become resistant to gemcitabine monotherapy and still deserve further therapy. This study is conducted to evaluate efficacy and tolerability of gemcitabine plus oxaliplatin as second line chemotherapy in gemcitabine pretreated advanced or metastatic pancreatic cancer patients.

Materials and methods: A total number of 35 patients were included with evaluable advanced or metastatic pancreatic cancer, between jan 2004 and jun 2005. The patients progressed on standard gemcitabine monotherapy. Median age was 58 years (range 28 - 73). Sex ratio M:F was 23:12. ECOG performance status was 0-2. The majority of patients had locally advanced disease and only 11 patients had metastatic disease. The treatment schedule was gemcitabine 1000 mg/sqm on day 1 and oxaliplatin 100 mg/sqm on day 2 repeated every 2 weeks. We evaluate the 6 months survival rate, the response rate and the toxicity of the regimen.

Results: All the patients received at least 2 series of chemotherapy. 18 patients survived at least 6 months after the initiation of the therapy (51.43%). Partial response was observed in 8 patients (22.86%) and stable disease in 11 patients (31.43%); the 16 remained patients progressed. The improvement of performance status (clinical benefit) was observed in 20 patients (57.14%). The regimen was well tolerated with grade 3-4 overall toxicity of 37.14% (leucopenia 17.14%, anemia 5.71%, thrombocytopenia 14.29%, emesis 5.71%, neurotoxicity 8.57%). There were no treatment related deaths.

Conclusions: This combination of Gemcitabine and Oxaliplatin has a moderate activity with acceptable and manageable toxicity in these pretreated patients. The clinical benefit justifies such approach in a selected category of patients with very limited treatment options.

1141 PRELIMINARY DATA OF SAFETY, TOLERABILITY AND EFFICACY OF ADJUVANT CHEMORADIOTHERAPY AFTER POTENTIALLY CURABLE SURGERY FOR LOCALLY ADVANCED GASTRIC CANCER. A SINGLE CENTER EXPERIENCE

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Background: Poor survival following optimal surgery of locally advanced gastric cancer suggest that adjuvant treatment is mandatory. Some studies showed that chemoradiotherapy significantly prolongs DFS and OS comparing with no adjuvant treatment.

Purpose: Evaluation of safety, tolerability and efficacy of combined chemoradiation after potentially curative surgery. Patients and methods: Out of 60 patients with gastric adenocarcinoma who undergone curative surgery in 2003-2005, 14 persons were selected for the evaluation after obtaining an informed consent, based on the pathological staging (pT3-4 or pN1-2 and M0), good PS (0-1) and no severe comorbidities. The patients were treated with the combination of chemoradiotherapy according to the protocol described by Macdonald et al. (NEJM 2001,345:725). Hematologic and non-hematologic toxicity were evaluated in relation to the WHO criteria.

Results: The most common adverse events were GI toxicity, especially nausea, anorexia and vomiting. No grade 4 GI toxicity was observed and G3 toxicity occurred only in 2 patients(1 subileus and 1 melena); G1-2 nausea occurred in 8 patients (61%), G2 vomiting was observed in 2 patients (15%). Hematological toxicity was rare and mild: G1 neutropenia occurred in 3 patients and G1 anemia in 2 persons; there were one G3 anemia, and one G3 thrombocytopenia. Only 2 patients had G4 neutropenia, including one G4 febrile neutropenia. All of these adverse events have resolved completely. Out of the 14, four patients died because of the disease progression (29% - metastases), and one from sudden cardiac death (7%) during the radiotherapy. Nine patients are alived, without disease progression. Median DFS was 16,5 months, and median OS was 17,6 months.

Conclusions: Combination of adjuvant chemoradiotherapy in locally advanced gastric cancer seems to be safe and well tolerated. Toxicity was transient and did not influence the treatment schedule. Too many progressions during the therapy and short DFS require selected changes of the regimen, perhaps intesification of the chemotherapy arm.

1142 IMPROVED MEDIAN SURVIVAL WITH PRE-OPERATIVE CISPLATIN, FLOUROURACIL AND INTERFERON ALPHA IN OPERABLE SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS

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Introduction: The combination of cisplatin, fluorouracil and interferon alpha has proven effective in advanced squamous cell carcinoma of the esophagus. We tested the feasibility and efficacy of this combination in the pre-operative setting for patients with operable squamous cell esophageal carcinoma

Method: Phase II trial. Patients who are considered potentially resectable by the surgeon were treated with 3 cycles of cisplatin 70 mg/m^2 IV on day 1, fluorouracil 500 mg/m^2 by continous infusion over 24 hours on days 1-5, and interferon alpha 4 million units/m^2 subcutaneously on days 1-5. Cycle repeated every 21 days. One level dose escalation was allowed if tolerated.

Result: Thirty patients recruited. Median age 59 years, median performance status 1. Twenty thre patients (87%) completed the planned 3 cycles of chemotherapy and 23 patients (77%) underwent radical esophagectomy. There was one toxic death. Grade 3 and 4 hematological toxicity were observed in 36.7 and 6.7% of patients. 4 of the resected specimens attained pathological complete response. With a median follow up was 17.4 months. The median time to progression was 6.8 months (95% CI: 5.2-10.9) and median overall survival was 26.3 months (95% CI: 5.29-47.5).

Conclusion: The above observed survival represent one of the best reported survivals for such groups of patients. We believe the above pre-operative combination should be tested in randomized phase III trials.

1143 BIOLOGICAL ASSESSMENT OF LIVER TOXICITY AFTER CHEMO-RADIOTHERAPY FOR DIGESTIVE TUMOURS WITH NO HEPATIC METASTASIS

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Objective: During treatment by chemo-radiotherapy of gastro-intestinal cancers, surrounding healthy organs could have alteration of their normal functions and especially biological parameters. Among the most sensitive organs are the kidney and the liver. For liver, above 25 Gy in a large part of the organ, symptomatic alteration may occur. However, dose - effect relationship for hepatic toxicity is not simple, as the liver is not homogeneously irradiated. Thus prediction of biological alterations after such a treatment and conversely, the interpretation of biological alteration in this context are difficult. To progress in the understanding of this biological process we studied the relations between the liver dose-volume histogram (DVH) and the importance of biological alterations.

Material and method: The retrospective analysis of the liver biological follow-up and the dose-volumes histograms of the treatments of all the elective patients, receiving a supra mesocolic chemo-radiation, between 1/2000 and 9/2005 has been done. Patients developing ultimately biliary retention or liver metastasis have been excluded. Biological abnormal thresholds were 2N for transaminases, 1,5N ALP and

gamma GT. The correlation between the different patterns of alteration of the biological results and the DVH data are studied.
Results: up to now, 121 medical records have been selected, 49 have been discarded because of the lack of treatment, liver metastasis or biliary obstacle, the premature death, or palliative treatment. So far 72 cases have been studied, 67 patients received chemotherapy, all of them but 2 (gemcitabine or carboplatine as monothérapie), received 5FU or an equivalent per-os, *with* a platinum drug in 20 cases. Radiotherapy was of 45-61 Gy. At the present time only 7 cases have fully available liver tests and DVH. The preliminary analysis of these data shows that the 4 persistent cases of elevated livers tests are associated with the highest DVH parameters: V25Gy / V30Gy are respectively 69/48; 70/57; 55/48 and 48/16%; and that the 3 without any biological alteration have V25Gy / V30Gy of respectively 58/36; 40/27 and 32/21%. This preliminary study is presently extended for better analysis.

1144 "EFFICACY AND TOLERANCE OF GEMCITABINE-BASED REGIMENS IN ELDERLY PATIENTS WITH ADVANCED PANCREATIC CANCER"

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Background: despite the emergence of gemcitabine use, patients with advanced pancreatic cancer (APC) have a poor prognosis. In elderly patients with APC, the use of gemcitabine, its tolerability profile and its efficacy remain poorly studied.
Methods: we retrospectively compared treatment efficacy (tumor growth control [TGC], time to progression [TTP], overall survival [OS]) and tolerability between patients < 70 years (group A) and patients (Pts) aged 70 years and older (group B) coming from prospective phase II and III studies performed between January 2001 and December 2004 in our department and treated with gemcitabine (GEM)-based first-line chemotherapy. The prognostic role of patients-, tumor- and treatment-related variables was assessed by univariate analysis (Log-rank test) and multivariate analysis (Cox proportional hazard model) focusing on the patients aged 70 years and older.
Results: a total of 99 patients (pts) (median age 66, range 27-87 years) were studied: group A=57 and B=42 treated by GEM alone (n= 61 pts) and GEM-based combination (n= 38 pts). TGC (partial response (PR) + stable disease (SD) >8 weeks) in first-line chemotherapy were 66.6% versus 59.6% (p=0,437) and TTP were 119 (88-150) versus 104 (111-224) days (p=0,846) for group A and B respectively. OS were 240 (95%CI: 118-312) and 220 (95%CI:85-355) days for group A and B respectively. A total of 42 pts received second-line chemotherapy (group A=14, group B=28). TGC and TTP were respectively for group A and B 57,6% versus 57,1% (p=0,978) and 74 (95%CI:35-113) versus 64 (95%CI:26-102) days (p=0,712).Grade 3-4 toxicity for group A/B: haematological toxicity: 24/23 (42.1%/54.7%), non haematological toxicity: 9/10 (15.7%/23.8%). Anemia: 5/6 pts (8.8%/14.3%, p=0.022) and neuropathy: 0/2 pts (0%/4.8%; p=0.003) were significantly more frequent for group B patients. No toxic death was observed in both group.
ALAT>53UI/l and KPS<90 at baseline were identified as independent negative prognostic factors for elderly patients.
Conclusion: TGC, TTP and OS were not statistically different between elderly and younger patients. ALAT and KPS could represent important prognostic factors in this population.

1145 ACCURACY OF IMAGING TECHNIQUES AND TUMOR MARKER CA 19-9 IN THE DIAGNOSIS OF PANCREATIC CANCER

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Purpose: Purpose of our study was to compare the diagnostic accuracy of different methods (imaging techniques and CA 19-9) for the differentiation of malignant from benign pancreatic lesions.
Patients and Methods: A total of 84 patients were evaluated. All patients with pancreatic lesions were examined by ultrasonography and magnetic resonance imaging. Ultrasound-guided biopsy was used to diagnose the pancreatic cancer. Carbohydrate antigen 19-9 level was measured in patients with suspected pancreatic cancer.
Results: Pancreatic cancer was diagnosed in 52 patients, benign pancreatic disease in 32 patients. Pancreatic lesions were identified and verified by ultrasound-guided biopsy, surgery or clinical follow-up. Chronic pancreatitis was diagnosed in 20, acute pancreatitis in 3, and benign digestive disease in 9 patients. Benign focal pancreatic lesions were identified in l1 patients. Suspected pancreatic cancer was found in 7 patients with ultrasonography and in 4 patients with magnetic resonance imaging. Magnetic resonance imaging did not identify focal malignant lesions in 4 patients with pancreatic cancer and tumor marker CA 19-9 was elevated in 3 of them (sensitivity, 75%). CA 19-9 was elevated in 1 patient with benign lesion. Tumor marker CA 19-9 was not elevated in 10 patients with focal benign disease (specificity, 90%).
Conclusion: Imaging techniques gave good results in the evaluation of pancreatic lesions. The problems with imaging diagnostics arise in certain cases to differentiate malignant from benign focal pancreatic lesions. Imaging techniques and identification of CA 19-9 allow better precision of diagnosis of pancreatic cancer.