Conclusions: The oxaliplatin combination chemotherapy showed promising activity. The overall toxicity was low in both arms, therefore no dose adjustments were performed. Based on these results it was recommended to extend the study (as planed per protocol) into a phase III trial with a planned accrual of 216 pts.

741 POSTER

Capecitabine-oxaliplatin (XELOX) in hepatocellular carcinoma (HCC): preliminary results of a multicentric phase II study (FFCD 0303)

V. Boige[1], J. Raoul[2], D. Hajage[3], O. Bouche[4], J. Blanc[5], J. Seitz[6], L. Bedenne[7]. [1]*Institut Gustave Roussy, Medicine, Villejuif, France;* [2]*Centre Eugene Marquis, Medicine, Rennes, France;* [3]*Institut Gustave Roussy, Biostatistics Unit, Villejuif, France;* [4]*University Hospital, Medicine, Reims, France;* [5]*University Hospital, Medicine, Bordeaux, France;* [6]*University Hospital, Medicine, Marseille, France;* [7]*University Hospital, Medicine, Dijon, France*

Background: There is no standard systemic chemotherapy for patients with advanced HCC. Evaluation of new drug combination is needed in this poor prognosis disease. The trial was designed to evaluate the efficacy of XELOX in HCC.
Material and methods: Inclusion criteria: patients with measurable HCC non suitable for surgery or percutaneous ablation; Child-Pugh A or B, CLIP <4. Every 3 weeks patients (pts) received: capecitabine 2000 mg/m^2 d1-d14, oxalipaltine 130 mg/m^2 d1. The main endpoint was tumor response.
Results: From December 2003 to September 2004, 50 pts were included in this phase II trial: 44 men, 6 women; median age (range) 68 years [24–82]; PS (OMS) 0/1/2: 22/25/3 patients; Child-Pugh score A, 42 pts and B, 8 pts; CLIP 0–1, 21 pts, CLIP 3–4, 29 pts. The median number of cycles was 6 [1 – 14]. Grade 3–4 toxicity: neutropenia: 2 pts, febrile neutropenia 1 pts, thrombopenia: 5 pts; diarrhea 8 pts, nausea/vomiting: 2 pts, mucitis, 1 pts; hand foot syndrome: 2; cardiovascular 2 pts. Grade 2 and 3 neuropathy was observed in 9 and 3 pts. There were two toxic deaths: one myocardial infarction and one neutropenic infection. Overall response (39 evaluable pts): partial response (3 pts), stable disease (29 pts). The intent to treat disease control rate (RP + SD) = 64% (IC 95% = 49–77%). Median PFS and OS were 4.8 and 9.3 months, respectively.
Conclusion: Capecitabine and oxaliplatine combination is feasible in patients with HCC and compensated cirrhosis. Despite a low response rate, this regimen provides an interesting disease control rate (64%) and overall survival (9.3 months) with manageable toxicity in non pre-treated advanced HCC patients.

742 POSTER

A prospective multicenter phase II trial of capecitabine plus oxaliplatin (CAPOX) in advanced biliary system adenocarcinomas

O. Nehls[1], H. Oettle[2], J.T. Hartmann[1], R. Hofheinz[3], H.G. Hass[1], A. Hochhaus[3], M. Makowski[2], D. Arnold[2], M. Gregor[1], B. Klump[1]. [1]*University Hospital Tuebingen, Internal Medicine, Tuebingen, Germany;* [2]*Charité, Campus-Virchow-Clinic, Hematology and Oncology, Berlin, Germany;* [3]*University Hospital Mannheim, Hematology and Oncology, Mannheim, Germany*

Objective: To evaluate the safety and efficacy of capecitabine and oxaliplatin combination therapy (CapOx) in unresectable or metastatic adenocarcinomas of the biliary system.
Methods: 62 pts (26M, 36F) were enrolled (median age, 63 yrs). Major eligibility: histologic proven, measurable disease, age $\leqslant$75 yrs, ECOG PS $\leqslant$2. A total number of 331 cycles (median: 5; range 1–16) of oxaliplatin (130 mg/m^2, d1) plus capecitabine (2000 mg/m^2, d 1–14) were administered 3 weekly for gallbladder carcinoma (GBC) (25 pts), extrahepatic (20 pts), and intrahepatic (17 pts) cholangiocarcinoma (CCC). Response rates were assessed according to WHO standard criteria. Clinical outcome was determined separately for pts with either GBC/extrahepatic CCC or intrahepatic CCC (mass-forming type).
Results: Grade 4 toxicities (WHO) were diarrhea in 1 pt (1% of cycles), thrombocytopenia in 1 pt (1%), leukopenia in 1 pt (1%), and fever in 2 pts (1%); grade 3 toxicities were nausea/vomiting in 1 pt (1%), diarrhea in 2 pts (1%), thrombocytopenia in 3 pts (2%), and fever in 1 pt (1%). Grade 3/4 peripheral sensory neuropathy (Lévis scale) was found in 13 pts (14%). Two pts were removed from study because of oxaliplatin-related allergic reactions. One patient died due to sepsis and another due to cerebral insult after the first treatment cycle, respectively. The overall disease control rate on 42 evaluable pts with GBC or extrahepatic CCC was 69% (complete response (CR), n = 2 (5%); partial response (PR), n = 8 (19%); stable disease (NC), n = 19 (45%)), whereas progressive disease (PD) was found in 13 pts (31%). In 17 evaluable pts with intrahepatic mass-forming CCC, we observed no CR or PR, but 5 pts (29%) had SD, and in 12 pts (71%) PD was encountered.
Conclusions: The CapOx protocol appears to be well tolerable and highly active for advanced GBC and extrahepatic CCC (disease-control rate: 69%), whereas clinical results might be poorer in the subset of intrahepatic mass-forming type tumors. Survival data will be presented at the meeting.

743 POSTER

Second primaries in patients with gastric cancer: clinical significance and treatment outcome

V. Skoropad, B. Berdov. *Medical Radiological Research Center of Russian Academy of Medical Sciences, Abdominal Dept., Obninsk, Russian Federation*

Background: We investigated (1) whether second primaries affect the treatment strategy and outcome of gastric cancer and (2) whether neoadjuvant radiation therapy in moderate doses increases the incidence of metachronous tumors.
Material and methods: Between 1974 and 2003, 941 patients with gastric cancer underwent curative surgery and were the subjects of the study. In 377 patients surgical treatment was used while in 564 patients it was combined with adjuvant radiotherapy. Intensive preoperative regimens (20–27 Gy/5–11 days) were used in 495 patients. In 69 patients both preoperative and intraoperative radiation therapy (IORT, 20 Gy) were used.
Results: Second primary tumors with extragastric location were observed in 62 (6.6%) patients including 22 cases diagnosed and treated before gastric surgery (median interval 11.5 years); 23 cases of synchronous tumors and 20 cases diagnosed and treated after gastric surgery (median interval 8 years). Among second malignancies colorectal cancer predominated (14 cases). Groups of patients with and without second primaries did not differ significantly concerning most prognostic factors except for T-stage ($p = 0.0004$). Curative treatment for the second tumor was performed in 53 (82%) patients, the most frequent treatment modality was surgery alone (23 cases) followed by multimodal (16) and radiotherapy (13). 5- and 10-year survival rates in patients with and without second primaries did not differ significantly ($p = 0.13$). A significant difference was seen in the cause of patients' death depending on the time of the second tumor appearance. When they were treated before gastric cancer none of them resulted in patients' death. In the case of synchronous tumors they were the cause of death in the half of the patients. Metachronous tumors were responsible for the patients' death in all the cases (12). In surgical group metachronous malignancies developed in 9 (2.4%) patients; in radiation therapy group – in 11 (1.9%) patients including 1 (1.5%) patient in IORT group.
Conclusions: Second primaries are seen in 6.6% of patients with gastric cancer and in 12.5% of patients with early gastric cancer. Second tumors are not the contraindication for the curative treatment of each of the lesions but they do significantly affect the prognosis of the treatment. Moderate doses of preoperative radiotherapy and its combination with IORT do not increase the incidence of metachronous tumors after curative surgery for gastric cancer.

744 POSTER

Hepatic arterial infusion of carboplatin mixed with degradable starch microspheres by using implanted reservoir in patients with advanced hepatocellular carcinoma

M. Yoshikawa[1], M. Sunaga[2], M. Ebara[1], H. Fukuda[1], S. Okabe[1], Y. Masuya[1], S. Yukizawa[1], H. Saisho[1]. [1]*Chiba University School of Medicine, Gastroenterology, Chiba, Japan;* [2]*Chiba University School of Medicine, Laboratory, Chiba, Japan*

Background: Hepatocellular carcinoma (HCC) is common cancer worldwide. Because HCCs are chemotherapy-resistant tumors, and current systemic therapy has been unable to prolong survival, hepatic arterial infusion chemotherapy is usually used for the treatment of multifocal bilobar tumors of the liver, not amenable to transcatheter arterial chemoembolization (TACE). The purpose of this study (a phase II study) was to determine the efficacy and toxicity of carboplatin mixed with degradable starch microsheres (DSM) in patients with HCCs and underlying cirrhosis.
Methods: Patients with histologically confirmed advanced HCCs not amenable to surgery, PEI (percutaneous ethanol injection) and TACE were eligible for the study. Other eligibility criteria included an age of 20 to 75 years; a stage of 4-A; adequate hematological, renal and liver function; and informed consent. All patients had associated liver cirrhosis, and were implanted an infusion catheter connected with a reservoir to the hepatic artery via the femoral artery by percutaneous method. Carboplatin (175 mg/m^2) mixed with DSM (175 mg/m^2) and Lipiodol (<3 ml) was administered as a single bolus injection from the hepatic artery through

the reservoir on an out patient basis, and repeated every 4 weeks. Patients continued to receive carboplatin emulsion until disease progression or the appearance of unacceptable toxicity including hepatic failure.
Results: Thirty-two patients were enrolled between January 2000 and December 2004. One patient deteriorated before receiving chemo infusion and was excluded from further evaluation. The average number of arterial infusions given during the follow-up period ranged from 3 to 31 (median, 13.7). Out of 31 eligible patients, 15 patients had partial responses, for an objective responses rate of 48.4%; 7 patients had no change, and 9 had progressive diseases. The median survival time was 17.7 months (95%c.i. 14.1–21.2 months). The cumulative survival rates were 76.6% and 47.2% for the periods of 12 and 24 months, respectively. The grade 3–4 toxicities (NCI-CTC) observed were leucopoenia (12.9%), thrombocytopenia (19.4%), and increased AST (3.2%).
Conclusions: Repeated hepatic arterial infusion of carboplatin mixed with degradable starch microsheres by using reservoir is active and well tolerated in patients with advanced HCC underlying liver cirrhosis.

745 POSTER

Final report of Phase I/II study of docetaxel and S-1 for patients with advanced gastric cancer

Y. Sakata[1], K. Yamaguchi[2], I. Hyodo[3], W. Koizumi[4], H. Narahara[5], T. Doi[6], Y. Komatsu[7], T. Kato[8], S. Saitoh[9], T. Akiya[10]. [1]*Misawa Municipal Hospital, Depertment of Medical Oncology, Aomori, Japan;* [2]*Saitama Cancer Center, Saitama, Japan;* [3]*National Shikoku Cancer Center, Ehime, Japan;* [4]*Kitasato Univ. East Hospital, Kanagawa, Japan;* [5]*Osaka Med Ctr for Cancer and Cardiovascular Disease, Osaka, Japan;* [6]*National Cancer Center East Hospital, Chiba, Japan;* [7]*Hokkaido Univ Graduate School of Medicine, Hokkaido, Japan;* [8]*Niigata Cancer Center, Niigata, Japan;* [9]*Aomori Prefectural Central Hospital, Aomori, Japan;* [10]*Gunma Prefectural Cancer Center, Gunma, Japan*

Background: This phase I/II study was conducted to evaluate efficacy and safety of new combined regimen with docetaxel (DOC) plus S-1 in patients (pts) with advanced gastric cancer (AGC). DOC and S-1 have different modes of actions respectively, and showed both of anti-tumor activities for AGC and synergistic effect in combined administration.
Methods: Eligibility criteria included; pathologically confirmed AGC, measurable lesions, PS 0–1, $\leqslant$1 prior chemotherapy, $\geqslant$20 years old, adequate organ functions and written IC. In phase I part, the dose of DOC was elevated from the starting dose of 50 mg/m^2 and S-1 dose was fixed to 80 mg/m^2. DOC was administered on day 1 and S-1 was administered orally on days 1–14 consecutively, and the treatment was repeated every 4 weeks. Identifying recommended dose (RD) of combined DOC+S-1, phase II part was started to evaluate the profiles of efficacy and safety of this combined regimen.
Results: 50 pts were enrolled in this study from 9/02 to 6/04. In phase I part, all 3 pts enrolled in the starting dose level showed intolerable toxicities (grade 3 neutropenia with infection in one pt and grade 4 neutropenia on day 8 during S-1 administration in 2 pts). Then the dose of DOC was de-escalated to 40 mg/m^2 and this dose level was determined as RD for phase II part. 46 out of 47 pts enrolled were eligible and evaluable for safety and efficacy, respectively. Pt characteristics were as follows; median age 65 (range 42–79), M/F 31/15, PS0/1 29/17, histological type intestinal/diffuse 29/17 and chemonaïve/pre-treated 25/21 pts. ORR, MST and 1 year survival rate were 45.7% (95%CI: 30.9–61.0%), 14.2 months and 56.6%, respectively. Common grade 3/4 toxicities were neutropenia (67.4%), leukopenia (41.3%), anemia (21.7%), and anorexia (21.7%). These toxicities were tolerable and manageable. No treatment-related death was observed. The interim results were presented at ASCO2005 meeting (Abstract 4064), and final and mature results will be presented at ECCO13 meeting.
Conclusions: This new regimen with DOC and S-1 showed manageable toxicities and favorable survival benefit to warrant a further phase III study with this regimen in pts with AGC.

746 POSTER

Oxaliplatin and Irinotecan in advanced gastric cancer. A multicenter phase II trial

E. Wöll[1], W. Eisterer[2], W. Hilbe[2], T. Kühr[3], K. Gattringer[4], R. Greil[5], A. Zabernigg[4], C. Baldinger[3], J. Thaler[3]. [1]*General Hospital St. Vincent Zams, Department of Internal Medicine, Zams, Austria;* [2]*University Hospital Innsbruck, Clinical Division of General Internal Medicine, Innsbruck, Austria;* [3]*Hospital Barmherzige Schwestern vom heiligen Kreuz Wels, Department of Internal Medicine IV, Oncology, Hematology & Immunology, Wels, Austria;* [4]*General Hospital Kufstein, Department of Internal Medicine, Kufstein, Austria;* [5]*University Hospital Salzburg, Department of Internal Medicine III, Division of Oncology, Salzburg, Austria*

Treatment options for advanced gastric cancer are limited therefore inclusion of novel substances is mandatory. Several agents have recently emerged as potential new options for advanced gastric cancer. The combination of Doxetaxel/Cisplatin and 5-FU showed high respons rates and a small survival benefit at the cost of increased toxicity. The aim of this study was to evaluate the safety, feasibility and efficacy of an Oxaliplatin/Irinotecan combination in patients suffering from unresectable, locally advanced and/or metastatic gastric cancer. Both substances show activity in gastric cancer as single agent or in combination with other drugs but the combination of Oxaliplatin and Irinotecan has not been evaluated in this setting. The combination of Oxaliplatin 85 mg/m^2 biweekly with Irinotecan 125 mg/m^2 biweekly was chosen for the present study since it has been shown in colorectal cancer that a biweekly dose of at least 85 mg/m^2 oxaliplatin is superior to a lower dose and toxicity of Irinotecan is much lower if given fractionated into two doses. Furthermore the Irinotecan dose below MTD considers concerns about increased toxicity of Irinotecan in gastric cancer patients. 43 patients with histologically proven unresectable and/or metastatic gastric adenocarcinoma and no previous palliative chemotherapy and/or immunotherapy were selected. Median age: 61 years (range 32 –81 years), male/female ratio: 24/19, PS 0:11 patients, PS <3: 32 patients, single metastatic site: 19 patients, multiple metastases: 19 patients, previously adjuvant radiochemotherapy: 4 patients. This outpatient regimen was generally well tolerated. Frequently reported adverse events (more than 20% of patients) were grade 1 or 2 and included neutropenia (44% of patients), thrombocytopenia (30%), anemia (77%), nausea 67%), diarrhea (51%), alopecia (35%). Grade 3 and 4 toxities included neutropenia in 2/43 pts., anemia in 3/43 pts., nausea in 2/43 pts., and diarrhea in 4/43pts. 3 patients were taken off-study due to toxicity (asthenia, nausea, reversible renal failure). Sensory neuropathy occurred only as grade 2 in 15%, no grade * toxicity was observed. 35 patients are assessable for response with 2 pts. (5.7%) showing a CR, PR in 19 pts. (54%), SD in 11 pts. (31%), PD in 3 pts. (8.6%). Final results on TTP and OS will be presented during the meeting.
Conclusion: Oxaliplatin/Irinotecan is a feasabile outpatient regimen with low overall toxicity and manageable side effects and a response rate within the range of other combination therapies and represents an alternative 1st line regimen.

747 POSTER

Final efficacy results of a neoadjuvant chemoradiation phase II trial: paclitaxel, carboplatin and 5-FU with concomitant 45 Gy radiotherapy for stage II-III oesophageal cancer

L. van de Schoot[1], M. van der Sangen[2], G. Creemers[3], O. Repelaer van Driel[4], H. Rutten[1], G. Nieuwenhuijzen[1,5]. [1]*Catharina Ziekenhuis, Surgery, Eindhoven, The Netherlands;* [2]*Catharina Ziekenhuis, Radiotherapy, Eindhoven, The Netherlands;* [3]*Catharina Ziekenhuis, Internal Medicine, Eindhoven, The Netherlands;* [4]*Maxima Medisch Centrum, Surgery, Eindhoven, The Netherlands;* [5]*On behalf of the collaborating hospitals of the Comprehensive Cancer Center, region South-East, The Netherlands*

Introduction: The outcome for patients with oesophageal cancer undergoing surgical resection with curative intention is poor. In an attempt to improve outcome, neoadjuvant strategies have been studied. Neoadjuvant chemoradiation is most promising. Pathologic complete response (pCR) rates of 20–30% have been published. We aimed to assess the feasibility and efficacy of a new treatment strategy, neoadjuvant chemoradiation followed by surgery in patients with stage II-III oesophageal cancer.
Methods: In the period from Jan 2002 – Nov 2004, 50 patients with a potential resectable stage II-III oesophageal cancer received chemotherapy with paclitaxel 175 mg/m^2 iv and carboplatin AUC 5 iv on day 1 and 22, 5-Fu 200 mg/m^2 on day 1 to 42 in combination with radiotherapy 45 Gy in 25 fractions starting on day 1. Surgery followed 6–8 weeks after completion of neoadjuvant treatment.