of those pts showed documented tumor progression within 3 weeks of last CPT-11 therapy.

Results: Pts characteristics: median age 56 yrs.; PS (WHO) 0: 0 pts; PS 1: 8 pts: PS 2: 2 pts. All pts had at least 1 tumor related symptom. Median number of organs involved: 3.

Treatment: 4 pts received DDP 75 mg/$m_2$dl, FU 1000 mg/m_2 continous infusion (Cl)d1-5,q3w; 5 pts: DDP 50 mg/m_2d1, FU 2.0–2.6 g/m_2 Cld1 + 8, Folinic acid (FA) 500 mg/m_2d1 + 8,q2w; 1 pt: DDP 120 mgd1, FA 100 mgd1-3, FU 1.5 gd1-3Cl,q3w. Median number of cycles given: 3.

Response rate: PR: 2 pts, NC: 4 pts. PD: 4 pts. After documented progression under CPT-11 the tumor control rate is 60%. Median time to tumor progression: 16 wks. Symptomatic improvement: 50%. Out of 3 pts who had PD as best response to CPT-11 (primary resistance) 1 achieved PR and 2 NC.

Toxicity: grade 2: mucositis 2 pts, diarrhea 1 pt. nausea and vomiting 5 pts, asthenia 3 pts; grade 3: mucositis 1 pt. grade 4: 0.

Conclusion: 2_{nd}-line DDP/FU after progression while receiving CPT-11 is an active combination and results in a tumor control rate of 60% and symptomatic improvement in 50%. DDP/FU and CPT-11 show a lack of cross resistance.

552 PUBLICATION

Continuous infusion 5-Fluorouracil with or without cisplatin for the treatment of advanced gastric cancer. Results of two consecutive phase II trials of the Spanish Group for Gastrointestinal Tumor Therapy (TTD)

A. Cervantes[1], M. Navarro[2], A. Carrato[2], J. Sastre[2], A. Anton[2], Jm. Vicent[2], Jm. Tabernero[2], J. Aparicio[2], P. Escudero[2], E. Díaz-Rubio[2]. *[2]Ttd Group; [1]University Hospital, Hematology And Medical Oncology, Valencia, Spain*

Advanced gastric cancer (AGC) has a poor outcome and chemotherapy has mainly a palliative effect. Despite many years of chemotherapy, there are no definite data to suggest that 5-FU alone is inferior to other treatment.

The TTD group carried out two consecutive phase II trials in patients with biopsy proven AGC with measurable disease, Performance Status (PS) < 3 and normal liver, kidney, heart and marrow fuction. In the first one 5-FU was given as a sigle agent in 48-hours continuous infusion (3 g/m(sub)2(/sub)) every week. In the second trial cisplatin (3 g/m(sub)2(/sub)) was added every 3 weeks to the same 5-FU schedule. Median age, pretreatment PS, previous surgery and median number of metastatic locations was similar for both groups. Toxicity was mild for both types of treatment. With infusional 5-FU 7% of patients suffered from CTC grade 3–4 toxicity. The addition of cisplatin induced 12% of grade 3–4 toxicity. In the first trial 89 patients were treated with 5-FU alone. Overall response rate (ORR) was 18% (10–26, CI at 95%), with 7% complete responses (CR). Time to progression (TTP) and overal survival (OS) was 4.8 and 6.9 months, respectively. In the second consecutive trial 130 patients were treated with 5-FU plus cisplatin. ORR was 47% (39–55, CI at 95%), with 4% CR. TTP and OS was 4.8 and 9.2 months, respectively. The addition of cisplatin increases significantly the proportion of responses (ORR), without affecting the complete response rate (CR). However, there are no differences in time to progression (TTP) in both treatments. Overall survival (OS) favors patients treated in the combination therapy trial. Though this is the highest survival obtained in four consecutive trials of the TTD group, the design of the study does not allow to check if this advantage is statistically significant.

553 PUBLICATION

MRI in the long term follow up of patients treated with chemo-radiation (CRT) for anal cancer

D. Tait[1], A. Dzik-Djuraz[2], J. Husband[2], J. Glees[1], S. Essapen[1], C. Abson[1], S. Brooker[1]. *[1]Royal Marsden Hosptial, Clinical Oncology, Sutton; [2]Institute of Cancer Research, Academic Dept. of Radiology, Sutton, United Kingdom*

Purpose: To assess MRI as a means of detecting early tumour recurrence and of describing the late normal tissue effects in the perianal soft tissue and femoral heads.

Method: 18 patients with squamous cell carcinoma of the anus, treated with chemo-radiation according to the UKCCR protocol, have had an MRI examination one year post completion of treatment. Small field of view axial and coronal T2 and STIR images were used to define the anal complex anatomically. Perianal distortion was scored nil to marked (0–3) and the presence of avascular necrosis (AVN) of the femoral heads documented.

Results: There has been no clinical evidence of recurrent disease as determined by clinical and endoscopic examination. The MR criterion taken to indicate local disease control was the absence of a focus of high signal intensity in T2 and STIR imaging, greater than 1 cm in size. No such foci were detected. The most striking feature in all cases was the low signal intensity of the anal and peri-anal complex. This low signal intensity is in keeping with a short T2 characteristic of fibrosis. This appearance was scored 1 in 9 patients (50%), 2 in 5 patients (28%) and 3 in 3 patients (16%). One patient was unable to tolerate the MR examination. No cases of AVN were seen.

Conclusion: By the given MR criteria, MR supported the clinical and endoscopic impression of local tumour control. No MR evidence of femoral head AVN was seen in this sample of patients. MR has highlighted the varying degrees of architectural distortion of the anal complex at one year post chemo-radiation. This discriminating morphological scoring of these changes will permit correlation with functional outcome. Yearly examination are ongoing for this purpose.

554 PUBLICATION

Quality of life as outcome parameter in gastrointestinal (GI) surgery EORTC-QLQ-C-30 and tumor specific modules

Ch. Schmidt[1], F. Reibe[1], T. Küchler[2], B. Kremer[1]. *[1]CAU Kiel, Allgemeine und Thoraxchirurgie, Kiel; [2]CAU Kiel, Referenzzentrum Lebensualität in der Onkologie, Kiel, Germany*

Quality of Life (QoL) has become an important issue in modern quality mangement to measure health outcome in tumor surgery. Since September 1998 patients with GI tumors have been assessed pre- and postoperativly for their health related Quality of Life in daily clinical routine in our department. Development of the QoL modules used in this trial takes time and is depending on specific guidelines given by the EORTC.

From 1987–89 in a prospective prestudy QoL in 74 patients with GI tumors was measured at the Dep. of surgery at the University hospital of Hamburg. In open interwiews patients were asked for symptoms before, during and after therapy. This list of symptoms was completed by consulting experts and literature review. All subjectivly experienced symptoms were worded into simple questions and tested for clarity. These modules were used in two main studies with 500 (300 + 200) patients from 1990–96. Patients answered the questionnaires one day before surgery (Z0), one day before discharge (Z1) and one year after radical surgical treatment (Z2). This main study was followed by a psychometric analysis to measure reliability and to reduce the number of Items on the questionnaire. Validity was asessed by medical criteria. The questionnaires presented show a good reliability and validity and can be filled out by patients in less than 20 minutes.

Developments of tumor specific questionnaires for patients with GI tumors according to the guidelines of the EORTC are presented. Results from our prospective and retrospective studies underline the good reliabilty and satisfactory validity of those GI-modules in combination with the EORTC-QLQ-C-30.

555 PUBLICATION

Adjuvant intraperitoneal chemotherapy with cisplatinum, mitoxantrone, 5-fluorouracil and calcium folinate in stage II–III gastric cancer

E. Topuz[1], F.N. Aykan[1], M. Basaran[1], K. Uygun[1], F. Tas[1], B. Sakar[1], P. Saip[1], D. Bugra[2], H. Camlica[1], A. Aydiner[1]. *[1]Oncology Institute, Medical Oncology, Istanbul; [2]Istanbul Medical Faculty, General Surgery, Istanbul, Turkey*

Despite numerous trials of postoperative chemotherapy following potentially curative gastric resection, the value of adjuvant therapy is uncertain. Adjuvant chemotherapy is not a standard therapy after complete gastric resection, but there are many trials evaluating the role of adjuvant therapy.

The feasibility, efficacy and toxicity of adjuvant intraperitoneal chemotherapy (IPCT) were evaluated in patients with stage II–III gastric cancer. After complete tumor resection, cisplatin 60 mg/m^2, mitoxantrone 12 mg/m^2, 5-fluorourasil 600 mg/m^2 and calcium folinate 60 mg/m^2 were administered in 2 L normal saline intraperitoneally via temporary or semipermanent catheter every 4 weeks for 6 courses to 39 patients and were not removed from the peritoneal cavity. Characteristics of patients were median age 50 (25–66), female 13, male 26, stage II 9 (23%) and stage III 30 (77%).

203 IPCT courses were given. Twenty-seven (69%) patients had received the total of 6 courses. The median number of IPCT courses received per patient was 6 (range 1–6). Toxicity grading was done according to WHO criteria. The toxicity was mild. Non-hematological toxicity included: grade

I–II mucositis in 1.4%, grade I–II nephropathy in 2%, grade I–II emesis in 33%, grade III–IV emesis in 2%, grade I–II abdominal pain in 19% and grade III–IV abdominal pain in 2% of courses. Catheter obstruction occurred in 3 patients with permanent catheter, and colon puncture in 4 patients with temporary catheter. No grade III–IV hematological toxicity has occurred.

Median follow-up was 16 months. There were 8 (21%) intraabdominal and 10 (26%) systemic recurrences. Metastatic sites were liver in 5 patients, lung in 1 patient and local + liver in 4 patients. Five patients died without determination of recurrence site. Twenty-one patients were dead and 16 patients are alive without evidence of disease. Median disease free survival (DFS) and overall survival (OS) were 13 and 16 months. Cumulative 3 year DFS and OS were 40.5% (SD ± 8.7) and 42.2% (SD ± 8.9) respectively.

IPCT seems feasible and tolerable, but its efficacy should be evaluated in randomized trials.

556 PUBLICATION

Gemzar (GEM) + Mitimycin C (MMC) in patients with advanced pancreatic cancer (APC)

I. Bazin[1], A. Garin[1], J. Bulat[1], M. Narimanov[1], D. Nosov[1], D. Titov[1], A. Popov[1], R. Nasyrova[1], S. Tjulandin[1]. [1]*Russian Cancer Research Center, Clinical Pharmacology, Moscow, Russian Federation*

Purpose: GEM is the new agent with activity in APC, and clinical benefit re-sponse is reported 26–45% pts. by several investigators. We assessed an effi-cacy of combination GEM + MMC in pts with APC.

Methods: 25 pts. (13 men and 12 women) with measurable APC were included in trial. The average age of the patients 58.5 age. Karnofsky PS was from 60 up 90 (60-10; 70-5; 80-9; 90-1). The most of pts have severe symptoms of disease: pain – 20, loss weight – 19, weekness – 19. Thirteen pts received palliative surgi-cal treatment. 16 pts were treated MMC 5–10 mg/m^2 i.v. day 1, GEM 1000 mg/m^2 i.v. 1, 8, 15 days. Nine pts received regimen MMC 8 mg/m^2 i.v. day 1, GEM 1000 mg/v2 i.v. 1, 8, 21, 29 days, The interval between the cycles was 2 weeks.

Results: 23 pts were evaluated for toxicity and 21 pts for efficiency. Two pts had early progressive disease. OR for combinations GEM + MMC was 38%.. The duration of effect varied from 8 to 29+ weeks. 11 pts have SD. During of chemotherapy clinical benefit response was observed in 60% pts. Toxicity gr. III–IV for 1-st regimen: neutropenia – 45.2%, trombocytopenia-54%, pulmo-nary toxicity 20%, it was a reason to correct regime, for 2-nd regimen: neutro-penia – 12.3%, trombocytopenia – 4%, pulmonary toxicity – 1 pts from 9, flu-syndrome – 38%, edema – 20%.

Conclusion: the combination GEM + MMC has shown efficiency in treatment of patients with APC. Clinical improvement was registred in 60% patients. Sec-ond regimen of treatment demonstrated satisfactory efficacy and less toxicity.

557 PUBLICATION

Clinical significance of estrogen receptors investigation in patients with atrophic gastritis and gastric cancer

N.E. Kushlinsky[1], Y.M. Stepanov[2]. [1]*Russian Oncological Scientific Center, Laboratory of clinical biochemistry, Moscow, Russian Federation;* [2]*State Medical Academy, Gastroenterology, Dniepropetrovsk, Ukraine*

Purpose: Estrogen receptors (ER) participate in regulation process of gastric mucosa (GM) functioning, as well as in the process of its blasto-mogenesis, thus stomach can be considered as a target for estrogens. In a perspective study GM estrogen reception characteristics in patients with atrophic gastritis (AG) and gastric cancer (GC) were evaluated.

Metods: 128 patients were examined: 80-with GC and 48 with AG. In all the cases X-ray and endoscopic diagnosis was verified morphologically. ER level in the tissues was detected with the radioligand method by Lippman and Huff.

Results: ER were detected both in GM of patients with AG and GC cytosol fraction. Their level varied from 10 to 236 fmol/1 mg of protein. In tumours the ER level was higher (85.0 &61617; 8.0 fmol/1 mg of protein) then ER level in GM in patients with AG (21.0&61617; 4.0 fmol/1 mg of protein).

Conclussion: GC characterized with higher estrogen reception then AG, that is probably due to transition of cancer cells to the pathological endocrine regulatory mechanism.

558 PUBLICATION

Phase II trial of epirubicin, uracil-tegafur and leucovorin (ELV) in advanced gastric cancer

J. Feliu[1], Y. Fernández[1], C. Jara[1], J. de Castro[1], C. García Girón[1], A. Cubillo[1], M. Cornide[1], E. Casado[1], E. Espinosa[1], M. González Barón[1]. [1]*S. Oncopaz Cooperative Group, Spain*

Purpose: Phase II trial to evaluate the therapeutic potential and tolerance of the combination epirubicin-UFT-leucovorin in advanced gastric cancer.

Patients: 33 untreated patients with histologically proven gastric adeno-carcinoma were included. The mean age was 60 years (35–73), there were 8 women and 25 men. ECOG performance status: 0 in 5 patients, 1 in 18 and 2 in 10. Two patients (6%) had a locally inoperable advanced tumor and 31 metastatic disease (11 in 1 site, 20 in two or more sites)

Treatment: Oral UFT 195 mg/m^2/12 h days 1–14, i.v. leucovorin 500 mg/m^2 day 1, oral leucovorin 15 mg/12 h days 1–14, i.v. epirubicin 75 mg/m^2 day 1. Courses every 28 days on an outpatient basis for a minimum of 3 courses. Therapy was maintained until progression or severe toxicity appeared.

Results: 3 patients had a complete response (9%) and 9 a partial response (27%), for an overall response rate of 36% (95% CI 17.5–67-5%). 207 courses were administered, a median of 6 per patient. The main toxicities were gastrointestinal and hematological. WHO grade 3–4 toxicities: nausea/vomiting 4 patients (12%), diarrhea 8 (24%), fever 2 (6%), mucositis 1 (3%), anemia 1 (3%). Median time to progression was 6 months and overall survival 9 months.

Conclusion: these results suggest that the combination epirubicin-UFT-leucovorin is active in patients with advanced gastric cancer with an accept-able toxicity.

559 PUBLICATION

Phase II study of gemcitabine in patients with nonresectable cancer of the biliary system

S. Kubicka, M.K. Tietze, L. Rudolph, M.P. Manns. *Dept. of Gastroenterology and Hepatology, Medical School Hannover, Germany*

The biliary-system shares the embryologic origin with the exocrine pancreas. Therefore we investigated the effect of gemcitabine in patients with non resectable cancer of the biliary system.

Methods: Between January '97 and September '98 21 patients with non resectable cancer of the biliary system were enrolled. Patients were treated with Gemzar 1000 mg/m^2 i.v. over 30 min once per week. The first cycle included 7 applications followed by one week rest. The following cycles consisted of 3 applications only, followed by one week rest. Staging was performed after each cycle. Only one patient received GEM as a second line chemotherapy, 20 patients were chemotherapy naive.

Results: The number of cycles applicated varied from 1 cycle to 7 cycles (median 3 cycles). Five patients achieved a partial remission (PR 24%) and 11 patients had a stable disease. Three out of 16 patients without an objective response had a clinical benefit, defined as >10% gain of performance status and/or body weight. So far, the median time to progression was 17.4 weeks in 12 eligible patients. Two patients are still in partial remission (35 and 10 weeks after beginning of treatment). One patient with a primary non-resectable CCC underwent surgery (R0-resection) after 5 cycles of Gemzar because of his partial response. One patient with progressive disease under high dose 5-Fu/leucovorin, developed a stable disease for 21 weeks. Overall the regimen was well tolerated. Side effects (WHO) included 10 cases of grade 2 leukopenia, 2 cases of grade 4 anemia, 4 cases of grade 2 flue like syndrome and 7 cases of grade 2/3 nausea. One patient developed a hemolytic-uremic syndrome which resulted in the withdrawl of the treatment.

Conclusion: Our results indicate that the treatment of cancer of the biliary system with GEM is effective, well tolerated and leads to clinical benefit of some patients.

560 PUBLICATION

Phase II trial of gemcitabine in advanced gallbladder cancer

J. Gallardo[1], B. Rubio, L. Orlandi, M. Fodor, M. Yañez, P. Salman, M. Ahumada. *Oncología, Hospital Clínico Universidad de Chile;* [1]*Oncología Clínica Alemana, Santiago de Chile, Chile*

Gallbladder cancer (GC) is the leading cause of death from malignant neoplasia in women in Chile. Most patients (pts) present locally advanced or metatastic disease, the median survival being only 12 weeks. Based