series of resectable gastric carcinoma (n = 616, April 1986–July 1995) to look for the results of surgical therapy in elderly patients.

Methods: One hundred twenty six patients older than 75 years (20.5% male, n = 69, female n = 57, mean age 77.8 ± 3.5 years) were operated. All patient data were retrospectively studied with special regard to perioperative morbidity, mortality and survival (Kaplan-Meier, log-rank-test, $p < 0.05$).

Results: The majority of patients had at least two risk factors (69.8%, n = 88) in particular cardiovascular and lung disease. 26 patients had no risk-factors. Of all resections, 62.7% (n = 88) were classified as curative resection (R0). Postoperative morbidity and mortality rates were 26.2% and 4.1% respectively. Median survival after resection was 45 ± 4.4 months with statistically significant differences ($p < 0.05$) for R-classification and tumor stage.

Conclusion: Due to improved perioperative management, resection of gastric carcinoma in elderly patients is the treatment of choice. Although these patients often have age-related cardiovascular and pulmonary risk factors, postoperative morbidity and mortality even after extensive resection is low. Survival rates are comparable to younger patients and the prognosis is best after R0 resection, which therefore should be the goal of surgery for gastric carcinoma in elderly patients.

1261 POSTER

Double biochemical modulation of cisplatin, leucovorin and 5-fluorouracil in advanced gastric cancer

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Purpose: This phase II study was designed to evaluate the activity, safety and tolerability of weekly cisplatin (CDDP), leucovorin (Lv) and 5-fluorouracil (5-FU) in patients (pts) with advanced gastric cancer (AGC).

Methods: Between 9/93 and 8/96 28 patients (pts) with AGC were treated with CDDP 33 mg/m^2 as a 1-hour infusion, Lv 300 mg/m^2 in bolus and 5-FU 500 mg/m^2 in bolus, days 1.8 and 15 every 28 days, in an outpatient clinic. All but one had measurable disease by CT scan. Median age was 58 years (range 44–79). Nine were female and 19 male. Six pts were performance status (PS) 0, 18 pts PS 1 and 4 pts PS 2. Thirteen pts had primary metastatic disease. 17 pts had liver metastasis. All were evaluable by WHO criteria for toxicity and 24 for response (4 pts died of intercurrent disease). A median of 4 cycles were given (−9).

Results: Intent to treat analysis (N:28): Three pts (11%) had CR, 12 (43%) had PR, for an overall response rate of 54% (95% CI: 36%–72%), and 5 (18%) pts had stable disease. Median survival was 45 weeks for all the group (range 2–170+). Severe toxicity included neutropenia grade 3 in 8 pts and grade 4 in 2 pts, thrombocytopenia grade 3 in one and diarrhea grade 3 in 2 patients. Minor toxicity was grade 1 neuropathy in 11 and grade 2 in 2; grade 2 stomatitis in 2; grade 2 diarrhea in 5; grade 1 asthenia in 3; grade 2 nausea and vomiting in 12. Eight pts required blood transfusion.

Conclusion: This outpatient regimen has showed remarkable responses with excellent tolerability in AGC, survival ranks equally with more toxic regimens.

1262 POSTER

Treatment of hiliar cholangiocarcinoma (Klatskin's tumour). Our experience

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Between 3/89 until 1/97, 50 patients (pts) (30 males and 20 females) with hiliar cholangiocarcinoma (HCC) have been treated in our Hospital. In 33 pts (66%) the treatment were a palliative cutaneus transhepatic biliary drainage tube (group 1). In 17 pts (34%), radical surgical resection were performed (group 2): 7, all of them with Bismuth IV, liver transplantation (LT) and the rest, biliary resection +/− partial hepatectomy. Combined chemotherapy (5Fluorouracil+ Mytomicin C) and radiotherapy was performed in 13 pts: 2 of group 1 and 11 of group 2 after surgical resection.

Results: Secondary complications to the treatment were: Group 1: 21 pts (64%) (15 cholangitis, 4 septic shock, 4 biliary blockage, 4 gastrointestinal hemorrhage, 4 pancreatitis). Group 2: 12 (70%) (4 abdominal abscess, 3 biliary fistulae, 2 septic shock, 3 others) without postoperative mortality. Median survival was: Group 1, 5 +/− 5 months (range 0–15); group 2, 17 +/− 14 months (range 0–51) ($p \approx 0.015$). Patients with LT had a median survival of 27 +/− 12 m (range 18–51) whereas pts with biliary resection 11 +/− 11 m (range 0–33) (non statistically significance).

Conclusions: Surgical resection is the treatment of choice for HCC, with a significance increase of survival without a high morbimortality. Although the number of pts is low, LT is an effective new approach to the treatment of Bismuth IV HCC.

1263 POSTER

Proposal for an international multi center study: E-cadherin mutationspecific antibody to detect exon deletion in diffuse type gastric cancer

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Background: E-cadherin, a membrane bound homophilic adhesion molecule, was shown to be mutated in diffuse type gastric cancer. Due to splice site mutations, Exon 8- and Exon 9-deletions were detected in 39% of the patients using RT-PCR and direct sequencing of the E-cadherin gene in malignant tissue. Monoclonal antibodies were subsequently generated against the fusion site of exon 8 and exon 10, that recognize only cells with exon 9 deleted E-cadherin, whereas wildtype E-cadherin is not recognized. On this basis a mutationspecific detection of malignant cells is possible. Due to the location of the mutated protein (transmembrane protein with presentation of the mutated part extra cellular) it might be a target for antibody based therapy. Additionally there are possibilities to prime the immune system to mutated protein by peptide vaccination.

Aim: Due to the small number of patients carrying the mutation we propose an international multi center study to evaluate:

1. Epidemiology of E-cadherin exon 9 deletion in high risk countries for gastric carcinoma 2. Prognostic impact of E-cadherin exon 9-deletions and possible correlation to clinical data 3. Planning of future trials concerning a) toxicological background of the underlying reason for the mutation and b) therapeutic approach using monoclonal antibodies, immunotoxins and peptide based vaccination.

1264 POSTER

Phase II study with 5-fluorouracil and Ginkgo Biloba extract in patients with pancreas CA

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Purpose: To evaluate the efficacy, tolerability and quality of life (QL) of 5-FU combined with Ginkgo Biloba extrakt (GBE 761 ONC).

Methods: 46 pts with pancreas ca were treated in a prospective phase II study. The treatment (day 1–6) was repeated every 3 weeks until PD. Response to therapy was evaluated after 2 and 4 treatment courses.

Results: At present 46 pts were included, 25 pts were evaluable for response up to now. All pts were assessed for tolerability and QL. We observed a complete response (CR) in 1 patient, a partial response (PR) in 1 patient, an no change (NC) in 12 patients and a progressive disease (PD) in 11 patients. 7 patients are still on study. 5-FU + GBE was well tolerated. The toxicity consisted mainly of myelosuppression and gastrointestinal symptoms judged as 5-FU related.

Conclusions: The combination 5-FU and GBE is well tolerated, the objective response rate is in the range already known from 5-FU alone therapy. Overall survival data presentation are in progress.

1265 POSTER

Teniposide, mitomicin C and cisplatin combination in treatment of advanced gastric cancer

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A pilot study was performed to assess the efficacy and toxicity of the combination – teniposide (Vm-26), mitomycin C (MMC) and cisplatin (DDP) in patients with advanced gastric cancer.

Patients and Methods: Twenty-four patients (Sex: M-14, F-10. Mean age 50.1.) with measurable advanced gastric cancer received MMC 5 mg/m2 i.v. 1 and 7 ds.; DDP 40 mg/m2 i.v. 2 and 8 ds.; Vm-26 60 mg/m2 i.v. 4, 5, 6 ds.. Interval 28 ds.. A mean number of cycles were four.

Results: 21 pts. are evaluated for response and toxicity. The overall response rate was 42.7% (CR-5/21 (14.2%); PR 6/21 (28.5%)). 6 out of

21 pts. (28.5%) had minor response or no change (NC) and 6 out of 21 pts. (26.9%) had progressive disease. Time to progression was 43.2 + 3.9 weeks (for pts. with CR and PR-54 ± 3.67 (n = 9); for NC-35.2 ± 9.5 (n = 6); for pts. with progressive disease 10.1 ± 6.4 (n = 6)).

Treatment toxicity: leucopenia-73.9% (grade III–IV – 14.2%); anemia-34.7%; thrombocytopenia-8.6%; diarrhea grade II – 18.5%; stomatitis and esophagitis – 7.4%; vomiting – 77% (grade III–IV – 58.8%); alopecia – 85.1%.

Conclusion: TMP combination has evident antitumor activity in advanced gastric cancer. The toxicity of this regimen is moderate.

1266 POSTER

Gemcitabine in advanced pancreatic cancer: A phase II trial

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Purpose: To assess clinical efficacy and safety of gemcitabine in advanced pancreatic cancer.

Methods: From April 1995 to December 1996, 24 consecutive pts (13 female and 11 male, median age 64 yrs) with pancreatic carcinoma entered this phase II study. ECOG PS was 0 in 6 pts, 1 in 8 pts, 2 in 6 pts, and 3 in 4 pts. 15 pts had metastatic and 8 locally advanced unresectable disease. 19 pts did not receive any previous treatment, and 5 received first line chemotherapy with 5-fluorouracil. Gemcitabine 1000 mg/m^2 was administered iv in 30′ in the first cycle once weekly for up to 7 weeks followed by 1 week rest; then in subsequent cycles, once weekly for 3 of every 4 weeks. The median number of cycles administered was 4 (range 1–10); 3 pts received only 2 doses because of early progression or refusal, but they have been included in the clinical efficacy analysis.

Results: 4 pts obtained partial response (16%) and 10 (41%) stable disease; 10 pts experienced progressive disease. PS improved in 11 pts (46%); analgesic consumption was reduced in 10 pts (41%). In the majority of pts, treatment was well tolerated and all pts were treated on an outpatient basis. Toxicity was mild and mainly consisted in moderate and quickly reversible myelosuppression: we registered 3 episodes of WHO grade III–IV thrombocytopenia and 2 episodes of grade 3 leukopenia. Grade 3 anemia was noted in 2 pts. Systemic toxicity was irrelevant with 7 pts complaining of fever (grade 1–2) and 7 of mild astenia during treatment.

Conclusion: We conclude that gemcitabine chemotherapy was very well tolerated and determined a significant clinical improvement with modest antitumoral activity in pts with advanced pancreatic cancer.

1267 POSTER

Gastro-oesophageal smooth muscle tumors: Treatment and analysis of prognostic factors

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Purpose: Gastro-oesophageal smooth muscle tumors show a variaty in clinical presentation and prognosis and the optimal method of treatment remains unclear.

Methods: We studied retrospectively the clinicopathological data to determine the effect of surgery, the time to recurrence and survival.

Results: Between 1986 and 1996 we treated 61 patients (27 ♂, 34 ♀) with a gastro-oesophageal smooth musle tumor [38 pts leiomyoma (LM) (62%): 15 pts low grade leiomyosarcoma (LMS) (25%); 8 pts high grade LMS (13%)]. Age ranged from 18 to 87; mean 59 years in LM and 61 years in LMS. The mean tumor diameter was 4.6 (1–11) cm in LM and 8.3 (3–18) in LMS. Patients often complained of abdominal pain (63%) and gastrointestinal bleeding (59%). In 15 pts the LM were asymptomatic. LMS were situated at the distal oesophagus (3 pts); at the fundus (10 pts); at the corpus (7 pts) and at the antrum (3 pts). Of the 23 LMS, 12 pts underwent a complete resection and 7 pts a microscopic incomplete resection. At a median period of 15 months, 4 of the 13 resected low grade LMS and 5 of 6 resected high grade LMS recurred, usually in the liver. The median survival was 66 (6–128) months in low grade LMS and 16 (2–48) months in high grade LMS. The overall 5-year survival was 35% (75% low grade LMS, 0% high grade LMS (p = 0.023). Age, sex, tumor size and site had no effect on survival. Differentiation and radicality had a significant prognostic effect (p = 0.02).

Conclusion: Prognosis of gastro-esophageal smooth musle tumors mainly depends on tumor grade and free surgical margins. Even after microscopic complete resection high grade LMS had a negative influence on the survival. Studies with adjuvant treatment such as intraoperative radiotherapy and chemotherapy are needed to improve these results.

1268 POSTER

Gemcitabine (GEM) and 5-fluorouracil (5 FU) in advanced pancreatic cancer: A GISCAD phase II study

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Purpose: In a randomized clinical trial (Moore, ASCO 96), GEM has been shown to be more effective than 5 FU, the most common drug used in advanced pancreatic cancer. GEM and 5 FU work in different ways to inhibit DNA and RNA synthesis: from a theoretical point of view, their combination could result in higher response rates. To test this hypothesis, a two stage phase II study was initiated in November 96.

Methods: End points: response rate, clinical benefit (Andersen, ASCO 94) and toxicity. If objective responses and/or evidence of clinical benefit were observed in at least 5 of 13 patients, further 30 patients should be accrued. Schedule was: Gem 1000 mg/m^2 and 5 FU 600 mg/m^2, weekly for 3 weeks every 4.

Results: Characteristics of the first 13 patients were: 10 male and 3 female; median age 57 years (range 47–72 years); 4 patients had locally advanced disease, 4 had metastatic disease and 5 both sites of disease. In these 13 patients, we obtained 1 partial response and 5 clinical benefits. Side-effects were mild: no gastrointestinal toxicity or grade 3–4 (WHO) hematological episodes were recorded. We observed only two episodes of grade 2 (WHO) leukopenia and 1 of thrombocytopenia.

Conclusions: These results allowed the starting of the second step. Up to day (February 97), 7 further patients have been enrolled.

1269 POSTER

Aortic-stop-flow-infusion (ASF) in patients with unresectable pancreatic cancer

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Purpose: Chemotherapy in patients with pancreatic carcinoma remains disappointing. A suitable method to achieve an effective drug-concentration in the target tissue without causing the side-effects of a high-dose systemic chemotherapy seems to be the isolated hypoxic perfusion of the abdomen (ASF).

Methods: In a two-year trial ASF was performed in 17 patients (5 female, 12 male) with unresectable pancreatic cancer. In general anaesthesia the separation of the abdominal organs from systemic circulation was achieved by transfemorally inserted balloon-catheters into the aorta and vena cava. The infusion of 40 mg of Mitomycin C was followed by a hypoxic perfusion over 20 minutes. Response was evaluated by CT-scan after 6 weeks.

Results: In 20 perfusions no toxicity-related deaths were observed. Nausea and vomiting (10 episodes WHO ≥ III) were the most frequent toxicities. In 5 patients (28%) a deep-vein thrombosis occurred. No partial or complete remission was observed, a disease stabilization was achieved in 3 patients. The median survival after ASF was 4.2 months (range 1.3–21) without a significant influence of metastatic disease.

Conclusions: Inspite of some hopeful reports about regional therapy in pancreatic carcinoma ASF did not influence response or survival and showed clinically relevant side-effects. Due to these disappointing results we decided to stop this trial.

1270 POSTER

ELFE (etoposide, folinic acid, 5-fluorouracil, and epirubicin) regimen in the treatment of advanced pancreatic cancer (APC)

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Purpose: Pancreatic carcinoma is generally considered a chemotherapy-resistant malignant neoplasm and to date there is no established chemotherapeutic treatment for patients with advanced disease. Many new combi-