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)

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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

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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

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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

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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

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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

on data demonstrating effectiveness of gemcitabine (GEM) in pancreatic carcinoma and the common embryologic origin of the exocrine pancreas and gallbladder, we decided to study the effectiveness of GEM.

Between July 1997 and February 1999, 20 pts with advanced GC were treated with GEM 1000 mg/m$_2$ i.v. for 30' weekly for 3 weeks out of every 4 in a phase II study. Patients were treated on an outpatient basis. All pts had measurable locally or metastatic GC with hystological proof; no prior chemotherapy; mean age, 50.8 years (38–68); 13 were females and 7 males. They all had performance status (WHO) 0–2, twenty were evaluable for toxicity and 16 for response (3 too early 1 dropped out). A mean of 4 courses were given (1–14). There was no complete response but 8 partial responses, for a global response rate of 50% (8/16). Mean follow-up was 23.8 weeks. The median survival time was 19 weeks; 40% of all pts survived longer than 6 months. Side effects were mild: no gastrointestinal toxicity or grade 3–4 (WHO) hematological episodes were recorded.

It is concluded that GEM appears to be highly active and well tolerated. This agent might have a significant clinical benefit not only on response rate and survival but on quality of life, which warrants new trials especially in combination regimens.

561 PUBLICATION

Continuous 120 hours-infusion (CI) of mitomycin C (MMC) as salvage treatment in progressive or rapidly recurrent gastric cancer (GC)

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Purpose: To evaluate the safety and therapeutic activity of continuously infused MMC in metastatic GC patients (pts) following first-line chemotherapy (ctx).

Methods: Pts were treated with MMC 20 mg/m^2 i.v. over a time period of 120 h followed by a 3-weeks rest. 22 pts were enrolled. All were assessable for toxicity and 20 pts for response evaluation. Pts characteristics: Median age: 63 years (39–76); Sex (m/f): 13/9; Karnofsky status: 70% (50–100); Previous ctx: Bolus 5-FU/FA n = 6 (27%), ELF n = 4 (18%), EAP n = 3 (14%), CI 5-FU/FA/DDP/paclitaxel n = 9 (41%); Resection of primary tumor n = 12 (55%); sites of metastases: hepar n = 17 (77%), locally advanced n = 10 (45%), peritoneum n = 13 (59%), pulmo n = 5 (23%), bone n = 3 (14%), lymph nodes 14 (64%).

Results: 1 CR and 5 PRs were observed (ORR: 27.2% [CI$_{95\%}$: 6.3–48.1%). The median response duration was 2.1 mort (range, 2–5), the median survival 3.6 mon (CI$_{95\%}$: 1.2–6.0); $\frac{1}{2}$-year survival rate was 30%. Responding pts had a statistically significant overall survival advantage (3.1 vs. 8.6 mon, p = 0.03). There was a trend of a prolonged survival in pts who had not received aggressive 1st line-therapy (p = 0.06). Thrombo- and leukocytopenia (WHO °III/IV) were observed in 4 (18%) resp. 2 pts (9%), and treatment had to be stopped early in 2 cases (9%).

Conclusion: CI of MMC over 5d was feasible on an outpatient basis revealing an acceptable toxicity. MMC demonstrated activity in advanced GC, pts but had only limited efficacy after platin/paclitaxel-containing ctx.

562 PUBLICATION

Chemoimmunotherapy protocol for advanced gastric cancer

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Introduction: Treatment of gastric cancer is still controversial. Modulation of 5-FU cytotoxicity with different chemotherapeutics and immunomodulators is still under investigation.

Material and Method: We tested in a prospective Phase II study a chemo-immunotherapy protocol in advanced gastric cancer patients. The regimen consisted of Cisplatin 50 mg/m^2 D1, 5-FU 375 mg/m^2 D1-3, Folinic Acid 20 mg/m^2 D1-3, IFN- a 2b 3Mio U sc. D1-3, every 28 d; and IFN- a 2b 3Mio U sc. 3 times weekly between the cycles. The treatment was given for 6–8 cycles. Twenty-four patients were included (18 males, 6 females). Mean age was 53.46 yr. (25–76). Five presented with locally advanced disease, and 19 had metastatic disease (Distant lymph nodes: 12, Liver: 5, Lung: 2). Initial performance status was 0: 3 patients., 1: 12 patients, 2: 9 patients. Response rate was 33% (1 CR, 7 PR). Median overall survival was 9 months (95% CI 4–14 months). The toxicity profile of this regimen was: G I-II Fever: 14 patients, G II Neutropenia: 3 patients, G I Renal toxicity: 2 patients. We conclude that, this regimen is well tolerated on an outpatient basis, and effective in advanced gastric cancer patients.

563 PUBLICATION

Survival after curative gastric resection

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Between December 91 and March 97, 55 patients submitted to curative gastric resection in the Clínica Oncológica I of the Portuguese Institute of Oncologie entered in a Phase III Clinical Trial of adjuvant chemotherapy with FAMTX. These are the results of a single institution experience. Overall 5-year survival rate was 57.4%.

In the control arm 5-year survival was 59.7%. In the FAMTX arm 5-years survival 55.7%. Pathologic staging was an important prognostic factor with a survival rate of 84.4% and 47.9% for stages II and III/IV respectively.

Conclusion:

(1) Pathologic staging is an important prognostic factor in curative gastric resection.
(2) Adjuvant treatment with FAMTX has no effect in survival.

564 PUBLICATION

Pancreatic carcinoma: Simultaneous radiochemotherapy with gemcitabine and cisplatin. A pilot study

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Purpose: to determine feasability and toxicity of simultaneous RCT using GEM & cDDP in a pilot study.

Methods: Between 4/98 and 1/99, 10 pts with locally advanced pancreatic carcinoma were recruited. 3d-conformal Rx was administered with 1.8 Gy SD daily. Primary tumor, metastatic nodes and high risk nodes were irradiated with a TD of 50.4 Gy, followed by a conedown to 55.8 Gy. Cx consisted of cDDP (20 mg/m^2 IV, d1–5 & 29–33) and GEM (600 mg/m^2 IV, d −2, 5, 12, 19, 26, 33, (40). Acute toxicity for Rx (RTOG) and Cx (NCI) were recorded.

Results: 18/20 courses cDDP could be administered (1/18 with 50% dose reduction). 54/68 courses GEM were given (1/54 with 50% dose reduction) Reasons for canceling Cx in almost all cases were leuco- a/o thrombopenia. Critical GEM courses were d12 & 19. Substantial acute toxicity: leucopenia 7/10 stage (st.) III; 2/10 st. IV; thrombopenia 3/10 st. III, 4/10 st. IV; upper GI tract (nausea, vomiting) 3/10 st. III, 0/10 st. IV; diarrhea 0/10 st. III/IV. One pt with combined leucothrombopenia st. IV had received COPP-ABV 10 yrs ago for Hodgkin's dz. 2/3 potentially resectable pts were assessed resectable at restaging. One of them was resected (R0), the other one refused surgery.

Conclusions: Simultaneous RCT (GEM/cDDP) is feasible, however hematotoxicity is substantial. Therefore Cx dose should be reduced. Efficacy in a neoadjuvant setting seems to be promising.

565 PUBLICATION

"Docetaxel-cisplatin, an effective palliativ therapy concept in advanced gastric carcinoma?"

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Objective: The aim of this study was to analyse the response rate, survival time, time to progression and toxicity for patients with advanced gastric carcinoma and therapy with Docetaxel and Cisplatin.

Patients/Methodes: From 1/97 to 1/99 we treated 47 patients (32 m., 15 f.) with a median age from 62.4 years (39–75 years) suffering from advanced gastric carcinoma 21 patients had a primary C. and 26 patients a recurrency. From the 47 patients 20 (42.5%) had liver metasases, 10 (21.2%) lymph-node metasases, 8 (17.1%) peritoneal carcinosis and 9 (19.1%) without metastases.

Treatment regime: 75 mg/m^2 Docetaxel, i.v., 1 h, day 1; 75 mg/m^2 Cisplatin, i.v., 1 h, day 1. The cycle was repeated at day 21 × 6.

Results: Of these 47 patients we analysed 43 patients. We observed 3 CR (6.9%), 13 PR (30.2%), 1 MR (2.5%), 14 SD (32.5%) and 12 patients with a progress (27.9%). The ORR was 17/43 patients (39.5%). The median survival time was 13.1 months and the time to progression in median 5.1 months. We observed haematological side effects ≥ grade III (WHO) 21.3% and a nadir after 5 to 7 days. Other side effects were nausea/vomiting ≥ grade III (WHO) 8.6% and alopecia ≥ grade III (WHO) 7.6%.