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%.

Conclusion: We conclude that the combination of Docetaxel and Cisplatin is well tolerated with a significant efficacy with regard to response rate and toxicity in advanced gastric carcinoma.

566 PUBLICATION

Preoperative treatment with chemotherapy and radiation therapy in undifferentiated embryonal sarcoma of the liver in childhood

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Hepatic Sarcoma is the cause of 13% of liver Tumors. In Childhood, 50 and 60% are between 6 and 10 years old.

We present a case treated with QT, RT and partial hepatectomy, followed for 25 months.

Case Report: Male, eight years old, evaluated initially in January of 1997. He presented with malaise, abdominal, diffuse pain and mass that occupied most of the abdomen, that grew very fast in a period of about three months. Karnofsky 60%. Lab: DHL: 982 UI, AFP: negative. Other studies normal. USG and CT: scan, Hepatic lumor 1700 cc, originated in the right hepatic lobule, bone marrow biopsy normal. Hepatic Arteriography: revealed a hypovascular mass, well delimited. Chest radiography normal. Needle biopsy: undifferentiated liver sarcoma (embryonal), with necrosis and extended hialinization. (DNA Index: aneuploid, DNA 2.60). Initiated with chemotherapy three cycles every 21 days (Docetaxel 100 mg/m^2; Doxorubicin 45 mg/m^2; Carboplatin 300 mg/m^2), with administration of (GM CSF) days 7–11 of each cycle. A partial response (60%), was obtained. Radiotherapy was initiated two weeks after the last chemotherapy course, it was administrated in 30 sessions, two sessions per day, reaching a total dose od 5040 cGy. The radiotherapy fields were diminished as the tumor responded to treatment. An additional cycle of chemotherapy with the same drugs a dose was administrated, and eight weeks later, a complete surgical resection was performed. In the pathologycal report there were no viable neoplasic cells, only extensive necrosis and degeneration. No additional treatment was administrated.

Results: Localregional control and no evidence of metastasic disease after 25 months of complete treatment. (percentile 80 per weight and length of 146 cm pc 90). Physical and neurological development has been normal. Toxicity was tolerable, grade 2 Leucopenia.

Conclusion: 1) The treatment with chemotherapy was effective, obtaining a 60% partial response. 2) The combination of Docetaxel, Doxorubicin, and Carboplatin, was well tolerated and no grade 3 and 4 was observed. 3) Radiotherapy increased the initial response to chemotherapy. 4) The surgical procedure resulted simple, locally radical without exposing the patient high risk procedure. 5) After 25 months there is no evidence of disease.

567 PUBLICATION

Relative effectiveness of gemcitabine in the treatment for pancreatic cancer – A pragmatic approach

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Purpose: In order to assess the overall value of new drug developments in cancer therapy, effectiveness may need to be considered in relation to interventions in other areas of healthcare. A pragmatic measure for assessing this is the number needed to treat (NNT). This measure is widely used in other therapeutic areas.

Methods: Published clinical trial data comparing gemcitabine and 5-FU were used as the basis for calculating NNTs using 12 month survival as the outcome of interest (1). The NNT is the inverse of the difference in event rates between the experimental and control interventions. This means of displaying the data usefully expresses the therapeutic effort required to get a therapeutic response.

Results: The 12 month survival rates for gemcitabine (18%) and 5-FU (2%) resulted in an NNT of 7 – if treating 7 pancreatic cancer patients with gemcitabine rather than 5-FU results, one additional patient will survive to 12 months compared with what would be achieved with 5-FU. Additionally, the NNT for achieving a "clinical benefit" was 6.

Conclusions: This is very favourable compared with other interventions which are routinely used in the UK NHS. The NHS drug costs in 1995 were 6 times more for cardiovascular disease than for malignant disease and certain common interventions had less favourable NNTs than we have shown for the use of gemcitabine in pancreatic cancer. NNTs are a useful and pragmatic alternative to QALYs and provide valuable information for decision makers.

[1] Burris HA, Moore MJ et al. Improvements in Survival and Clinical Benefit With Gemcitabine as First-Line Therapy for Patients with Advance Pancreas Cancer: A Randomized Trial. J Clin Oncology 15 (6): 2403–2413, 1997

568 PUBLICATION

Prostaglandins E in patients with atrophic gastritis and gastric cancer

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Purpose: Atrophic gastritis (AG) is consided to be the phone disease and pathological state, which may result in gastric cancer (GC) development, especially in metaplastic and displastic changes of gastric mucosa (GM). Prostaglandins E (PgE) play important role in the maintenance of morphofunctional homeostasis of GM and determine its resistance to destructive impact of exogenous and endogenous factors. Recently, new data concerning PgE participance in the promotion of gastrocancerogenesis have appeared. The comparative investigation of PgE levels in GM bioptats in patients with AG and tumor tissues in patients with GC for detection of their characteristic conformity, is proposed.

Methods: 106 patients were examined (44 with AG, 62 with GC). X-ray and endoscopic diagnosis was verified morphologically in all the cases. The PG level in tissues was detected radioimmunologically with the reactive set "Clinical Assays‰ (USA)

Results: PgE level varied from 0.5 ng/g to 16.0 ng/g in GM bioptats in patients with AG and from 0.5 ng/g to 29.9 ng/g in tumor tissues. Mean PgE level was higher in tumors (9.3 ± 0.6 ng/g) than in GM bioptats in patients with AG (5.5 ± 0.7 ng/g). Direct correlation between PgE level and age of the patients as well as GM metaplasia degree in patients with AG was revealed.

Conclusion: AG progress is accompanied with PgE accumulation in GM. It may serve as an additional criterion of possibility of GM cancer transformation

569 PUBLICATION

Pseudomyxoma peritonei (PMP): The Portuguese Institute of Oncology – Oporto Centre experience

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Background: PMP it's a rare entity, characterised by an accumulation of extracellular mucin diffusely involving both peritoneal surfaces. It is still poorly understood. Peritoneal dissemination occurs in most patients (pts) but invasion of abdominal organs and distant metastases are rare.

Objective/Methods: To retrospectively evaluate the clinicopathologic features of the PMP pts treated in our Institution, between 1986 and 1998. Patients demographic data and turnout characteristics were studied. Six of the seven cases coded as PMP were reviewed.

Results: PMP was diagnosed in seven pts, four males and three females. The average age was 66 ± 9 years (Range: 50–73). Average follow-up, was 24 months (ms). The most common presentation forms were abdominal pain and distension. In all pts a mucinous cystadenoCa was found. In five pts the origin was appendiceal. No pt had extra-abdominal involvement. Surgery was the initial treatment in all pts. Three pts received intraperitoneal chemotherapy (CT), with one stabilisation and two progressions of disease but without extra-abdominal extension. One pt, treated with systemic CT, had stabilisation of disease. One pt was lost for follow-up, four are alive with evidence of disease and two pts, treated only with surgery, died. Average overall survival was 214 ± 20 ms (Range: 1–59).

Comments: 1) PMP is a very rare indolent malignancy that may remained confined to the abdomen for a long time. 2) Its most frequent origin is appendiceal. 3) CT after cytoreduction surgery may contribute to a better local control of disease. 4) Despite its persistence, overall survival is usually greater than in other forms of peritoneal carcinomatosis.