

13 m, and it has not been reached yet for the CRT group. Grade 3/4 toxicity (nausea, vomiting, diarrhea) during CRT was noted in 3 pts, and neutropenic fever in one.

Conclusion: This schedule of GEM and RT is well tolerated and can provide prolonged CB response and local control in pts with localized, unresectable pancreatic cancer.

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PUBLICATION

Significant improvement of response rate and survival with cisplatin, epirubicin, 5-fluorouracil and gemcitabine (PEF-G regimen) in metastatic pancreatic cancer

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Purpose: To assess the efficacy of PEF-G regimen by comparing response rate (RR), time to treatment failure (TTF) and overall survival (OS) with three other chemotherapy (CHT) regimens in metastatic (M1) cancer of exocrine pancreas.

Methods: In the period 1981–98, four consecutive clinical prospective trials were performed in 114 patients selected according to the following criteria: histologic diagnosis of exocrine pancreatic cancer; M1 disease; age 18–70 years; ECOG PS < 2; normal bone marrow, hepatic and liver function; no previous CHT. Twenty-two patients (1981–88, median age 59 ys) received FAM regimen (5-fluorouracil 600 mg/m² days 1, 8, 29 and 36; adriamycin 30 mg/m² days 1 and 29; mitomycin 10 mg/m² day 1); 41 patients (1989–93, median age 55 ys) were treated with EF (epirubicin 50 mg/m² day 1; 5-fluorouracil 1 g/m² days 1 to 5); 22 patients (1994–96, median age 58 ys) received PEF (EF plus cisplatin 50 mg/m² day 1) and 29 patients (1997–98, median age 58 ys) received PEF-G (cisplatin and epirubicin 40 mg/m² day 1; 5-fluorouracil 200 mg/m²/day continuous infusion and gemcitabine 600 mg/m² days 1 and 8). All patients enrolled were considered for an intent-to-treat analysis. Response to CHT was assessed every 2 courses by CT scan.

Results: PEF-G compared favourably with the other three regimens for RR, TTF and OS, while no significant differences were detected among FAM, EF and PEF.

	FAM	EF	PEF	PEF-G	p
CR + PR (WHO criteria)	9%	2.5%	13.5%	62%	<0.0001 [†]
Median TTF (months)	2	2.5	2.5	5	0.0002 [°]
6 months progression-free	5 + 4%	10 + 5%	29 + 10%	42 + 11%	
Median survival (months)	5	5	7	6.5 +	0.009 [°]
1-yr survival rate	9 + 6%	9 + 5%	5 + 5%	27 + 11%	

([†] chi square [°] log-rank)

Conclusions: Even if these results should be confirmed in a larger series, PEF-G seems to be more effective than other CHT regimens in metastatic pancreatic cancer. Due to the significant improvement in RR, TTF and OS, PEF-G could become the first choice CHT regimen in pancreatic cancer.

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PUBLICATION

Periampullary carcinoma: Impact of adjuvant chemoradiotherapy on outcome

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Purpose: To evaluate the role of adjuvant chemoradiotherapy in periampullary carcinoma.

Methods: From 1989–1998, 66 patients of periampullary carcinoma were evaluated. All the patients underwent whipple's procedure. 45/66 (68%) patients received post-op adjuvant chemoradiation. Radiotherapy was given in doses of 45–50 Gy/4–5 wks with 5-FU 500 mg IV weekly × 12 wks. The patients with histological features of poorly differentiated, positive resection margin, lymph node & infiltration into pancreas were considered as high risk.

Results: 5-year estimated overall survival was 26% in adjuvant group versus 11% in surgical group. High risk patients with chemoradiation had 5-year survival of 16% vs 5% surgical group.

Conclusion: High risk group patients had high local failure rate and so require post-op adjuvant therapy. A prospective randomized control trial is needed for confirmation.

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PUBLICATION

Long term results with the surgical treatment of resectable gastric cancer

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Surgery remains as the only effective treatment of gastric cancer. Between January 1986 and December 1990, 279 patients were treated in the Clinica Oncologica I of the Portuguese Institute of Oncology-Porto

Fifty eight per cent were male and 42% female. Age was over 60 years in 65% of the patients.

Tumor location was: distal 1/3 – 103, middle 1/3 – 47, proximal 1/3 – 66, diffuse 63. The predominant treatment was surgery in 228 cases, chemotherapy in 10 cases and symptomatic in 41 cases.

Results: The overall 5-year survival rate was 48% for patients submitted to gastric resection. Depth of the tumor was an important prognostic factor with a 5-year survival of 90%, 70% and 32% for T1, T2 and T3, respectively. Lymph node metastasis was also a significant prognostic factor with a 5-years survival of 72% for N⁻ and 22% for N⁺. Location of the tumor and type of surgical resection do not alter the prognosis.

Conclusion: Gastric resection is a potentially curative procedure and is compatible with a long term survival.

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PUBLICATION

Submucosal tumors of the esophagus: Diagnostic role of endoscopic ultrasonography

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Background and Aims: The diagnosis of submucosal tumors of the esophagus by endoscopic ultrasonography (EUS) is based on their relation to the five-layer sonographic pattern of the normal esophageal wall produced by a radial scan transducer. Preliminary reports have suggested that this modality may be useful in imaging the esophageal wall more accurately than other imaging techniques. The aim of this study was to define the usefulness of EUS in the diagnosis of submucosal tumors of the esophagus and in the determination of their size, location and histological nature.

Patients and Methods: From June 1997 to January 1999 at the Endoscopy Service of the Institute of Clinical Oncology – University of Messina, 23 consecutive patients, 13 males and 10 females, ranging from 36 to 71 years of age (median age 56.1), with endoscopically proven esophageal submucosal tumor, were included in this study. We use an ultrasound endoscope with a radial-scan transducer which offers a choice of 7.5 MHz or 10 MHz scanning frequencies (Olympus GF-UM2/EUM2).

Results: Using EUS we diagnosed 21 cases of leiomyoma and 2 cases of leiomyosarcoma confirmed histologically. The EUS appearance was that of a hypoechoic mass arising in the fourth hypoechoic layer corresponds to the muscularis propria. Tumor diameter ranged from 5 to 35 mm. In all two cases of leiomyosarcoma, the size of the tumor was larger than 20 mm in diameter. No complication was encountered during this study.

Conclusions: Our findings are in accord with the existing literature and confirm the usefulness of EUS in the evaluation and in the diagnosis of submucosal tumors of the esophagus. In particular, due to its definition power, it gives accurate informations about size, location and nature of the esophageal intraparietal lesions.

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PUBLICATION

Cisplatin /5-FU (DDP/FU) as 2nd-line chemotherapy after CPT-11 (Irinotecan) failure for patients with metastatic gastric adenocarcinoma

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Purpose: Currently there are no data for chemotherapeutic options after tumor progression during CPT-11 therapy for metastatic gastric adenocarcinoma (MGC).

Method: A retrospective analysis was performed to determine the response rate and symptom control of pts with MGC treated with a 2nd-line DDP/FU combination after tumor progression while receiving CPT-11 single agent as 1st-line therapy. Data from 10 pts could be evaluated so far. All

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/m²dl, FU 1000 mg/m² continuous infusion (CI)d1-5,q3w; 5 pts: DDP 50 mg/m²d1, FU 2.0-2.6 g/m² Cld1 + 8, Folinic acid (FA) 500 mg/m²d1 + 8,q2w; 1 pt: DDP 120 mgdl, FA 100 mgdl-3, FU 1.5 gdl-3CI,q3w. Median number of cycles given: 3.

Response rate: PR: 2 pts, NC: 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: 2nd-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.

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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)

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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 function. In the first one 5-FU was given as a single agent in 48-hours continuous infusion (3 g/m²(sub)2/(sub)) every week. In the second trial cisplatin (3 g/m²(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 overall 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.

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PUBLICATION

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

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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 UKCCF 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.

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PUBLICATION

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

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Quality of Life (QoL) has become an important issue in modern quality management to measure health outcome in tumor surgery. Since September 1998 patients with GI tumors have been assessed pre- and postoperatively 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 interviews patients were asked for symptoms before, during and after therapy. This list of symptoms was completed by consulting experts and literature review. All subjectively 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 assessed 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 reliability and satisfactory validity of those GI-modules in combination with the EORTC-QLQ-C-30.

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PUBLICATION

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

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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/m², mitoxantrone 12 mg/m², 5-fluorouracil 600 mg/m² and calcium folinate 60 mg/m² 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