1 gm/m^2 on days 1–4 and days 29–32 and a bolus dose of mitomycin C 10 mg/m^2 on day 1.

Results: A total of 96 patients satisfied the inclusion criteria, 70% female. The median age was 62 years (range 33–86). T stages at presentation were: Tx 2%, T1 18%, T2 50%, T3 9%, T4 21%. Thirteen patients (14%) had involved inguinal nodes. Disease persisted after chemoradiation in 10%. At 10 years following commencement of radiotherapy a further 19% were estimated to have suffered locoregional relapse, 6% distant metastases and 19% death without known progression, leaving 46% surviving failure-free at 10 years. Estimated overall survival was 91% at 2 years, 72% at 5 years and 59% at 10 years. There were no significant differences in failure-free survival between T stages-T1, T2, T3, T4, between N0 and N1–3, between T1–2N0 and T3/T4/N1–3. Patients with tumours <4 cm survived significantly longer without failure than patients with larger tumours (P = 0.006). In terms of overall survival, there were no significant differences between T stages, between N0 and N1–3, between T1-2N0 and T3/T4/N1–3, or between <4 cm and >4 cm tumours.

Conclusion: In our experience, TNM stage for carcinoma of anus does not predict failure-free survival or overall survival in patients treated with chemoradiation.

514 POSTER

A phase II study of hypofractionated radiotherapy in combination with Gemcitabin in the palliative treatment of advanced pancreatic carcinoma

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Purpose: To evaluate the toxicity and palliation of hypofractionated radiotherapy in combination with gemcitabine in advanced inoperable pacreatic carcinoma.

Patients and Methods: A total number of 21 patients with recurrent disease after resection, primary irresectable and/or metastatic tumours were included. Gemcitabine (300 mg/m^2) was given at day 1, 8 and 15 at the same day of radiotherapy. CT-assisted radiotherapy consisted of 3 fractions of 8 Gy, once a week on the macroscopic tumour. From day 22, gemcitabine (1000 mg/m^2) was continued weekly. The mean number of courses was 12 (3–21). Al most all patients suffered from intractable abdominal pain.

Results: Treatment was generally well tolerated. Seventeen patients experienced mild nausea and vomiting and 7 patients experienced mild abdominal pain. In 7 patients, an increase of pre-existing pain was noted shortly after radiation. In 1 patient gemcitabine was not given before the third fraction because of hematological toxicity and in 6 patients dose reduction was needed. No significant changes of liver enzymes and renal function were noted. A significant reduction of the tumour marker CA 19.9 was observed in 14/17 patients (82%). Palliation of pain was observed in 13/18 patients (72%). Pain medication could be reduced in 11/15 patients (73%). The median survival was 16.2 months.

Conclusion: Hypofractionated radiotherapy in combination with gemcitabine in irresectable pancreatic carcinoma is well tolerated and offers good palliation.

515 POSTER

Phase I/II study of irinotecan combined with mitomycin-C in patients with advanced gastric cancer

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Purpose: Irinotecan (CPT-11) is a new active drug for advanced gastric cancer (AGC). Preclinical synergism has been reported in combination of CPT-11 and mitomycin-C (MMC) in human gastric cancer cell lines. To determine the maximum tolerated dose (MTD), the dose limiting toxicity (DLT), and preliminary anti-tumor activity, we conducted a dose escalation study of CPT-11 and MMC in patients with AGC.

Methods: MMC was administered as i.v. bolus, and then immediately followed by intravenous infusion of CPT-11 over 90 minutes. The treatment was repeated every other week. Granisetron was administered to prevent nausea and vomiting. The prophylactic use of granulocyte colony-stimulating factor was not planned. The planned dose escalation schedule for MMC/CPT-11 (mg/m^2) of each dose level was as follows; level-1, 5/100; level-2, 5/125; level-3, 5/150; level-4, 7/150; level-5, 10/150. MTD is determined when the incidence of critical toxicity (either grade 4 neutropenia "4 days, febrile grade 4 neutropenia, non-hematological toxicity "grade 3, or treatment delay due to any toxicity >7 days) exceeds 50% (2/3 or 3/6 patients).

Results:: Twenty-one patients was entered (3 at level-1, 7 at level-2, 6 at level-3, 3 at level-4, and 2 at level-5, respectively) and 20 patients were evaluable for toxicity. Patient characteristics were following; median age 61 yrs [range 46–73]; sex 18 male, 3 female; PS 0–4, 1–15, 2–2; macroscopic type; diffuse –4, non-diffuse –17; microscopic type; diffuse –19, intestinal –2. At level-1, no critical toxicity was observed. At level-2, the critical toxicity was observed in 2 of 7 patients (administration delay due to persistent leukopenia and grade 4 diarrhea). At level-3, the critical toxicity was observed in 2 of 6 patients (grade 4 neutropenia "4 days and grade 3 diarrhea). At level-4, no critical toxicity was observed. At level-5, the critical toxicity was observed in 2 patients (administration delay due to hematological toxicity and grade 3 diarrhea). At the present, partial responses were achieved in 8 of 16 patients evaluated (response rate; 50%). In eight chemotherapy-naive patients, partial responses were obtained in 6 patients (response rate; 75%). The chemotherapy could be continued on the outpatient-basis in all patients.

Conclusions: We determined that the maximum tolerated dose of CPT-11 and MMC was 150 mg/m^2 and 10 mg/m^2, respectively and that the recommended dose of CPT-11 and MMC for a phase II trial was 150 mg/m^2 and 7 mg/m^2, respectively. Additionally, the present study suggested the combination chemotherapy with CPT-11 and MMC should be very active against advanced gastric cancer. We will soon start a phase II study of this regimen.

516 POSTER

Stage-adapted radio-chemotherapy in anal canal carcinoma

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Purpose: The optimal combination of radio-chemotherapy in anal canal carcinoma has yet to be established. The advantages of stage-adapted therapy and the merits of different radio-chemotherapy combinations in advanced stages are analyzed.

Methods: 56 patients with anal canal carcinoma with a median age of 64 years (range 29–92) were treated. Median follow-up was 28 months (range 10–75 months). 8 patients with early stages received only local irradiation up to 60 Gy, 19 patients with T2 N0 stages were treated with a combination of 5-FU and 50 Gy, 29 patients with advanced stages received 50 Gy combined with 5-FU and Mitomycin C (14 patients) or 5-FU and Cisplatin (15 patients).

Results: Overall-survival was 80%, disease-survival 60% at 5 years. The local recurrence rate was 22%. None of the patients treated with a combination containing Cisplatin developed distant metastasis as compared to 36% in the Mitomycin C group.

Conclusion: Early stage patients can be successfully treated with irradiation alone or combined only with 5-FU. Advanced cases seem to profit more from a combined radio-chemotherapy regimen containing Cisplatin.

517 POSTER

Hepatocellular carcinoma: Adjuvant chemotherapy postliver transplant

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Background: Transplantation is sometimes recommended for hepatocellular carcinoma (HCC). Patients with cirrhosis in stage II to IVA have a median survival of 12 months following surgical resection or other local therapies. More than 86% of patients have a recurrence within the following 2 years. Liver transplantation has been occasionally used in these patients, with or without complementary chemotherapy.

Materials and Methods: Between 1992 and 1998, 9 patients underwent transplantation and subsequently received weekly doses of adjuvant doxorubicin 10 mg/m^2, for 20 weeks. All patients had hepatocarcinoma. Eight patients had cirrhosis (44.4% C virus, 0% B virus, 22.2% alcoholic, 22.2% cryptogenic, 0% metabolic hepatopathy). One patient had chronic active hepatitis. Classification was 33.3% stage II, 22.2% stage III, and 44.4% stage IV-A. Major vascular invasion was seen in 11.1%, microscopic invasion in 22.2%, and 44.4% had capsular invasion (11.1% pT2). Single tumorous nodules were found in 33.3%, multiple tumorous nodules in 1

lobe 22.3%, and 44.4% multiple tumorous nodules in both lobes. 44.4% had incidental operative HCC. The larger nodules had a median diameter of 4.5 cm. Median Child and Pugh classification was B-7. Median αfetoprotein level was 16. Median prothrombin time was 70%. Median patient age was 57 years. Male/female ratio 3:1. Median ECOG was 1. Two patients received preoperative treatment: 1 underwent PIE and tamoxifen, and 1 chemoembolization. Mean time from transplantation to chemotherapy was 25 days. Ventricular heart function was not monitored because no patient received doxorubicin dosage in excess of 200 mg/m^2 and there was no previous cardiopathy in the enrolled patients.

Results: 66% patients received full dosage and completed the scheduled treatment. 22% had 25–50% dose reductions for myelotoxicity (grade III–IV). 1 patient (11.1%) had treatment withdrawn due to toxicity after 12 doses (P. Carinii and CMV pneumonia). There was 1 treatment related death (P. Carinii pneumonia at 4 months). Reduced immunosuppression doses were administered to 4 patients during chemotherapy due to high serum levels. 4 patients relapsed (44.4%), 1 in the first year, 3 in the third year. 2 patients died without evidence of tumor (1 of pneumonia and 1 of acute Epstein-Barr hepatitis), and 3 patients are still living without evidence of disease at 4, 13 and 14 months. C virus recurrence occurred in 1 patient. Median survival following transplantation was 14 months (4 to 37 months).

Summary: Liver transplantation combined with doxorubicin adjuvant chemotherapy is a feasible treatment in hepatocarcinoma-cirrhotic patients and seems to have a moderate effect in survival in this group of patients.

518 POSTER

Localised squamous – cell cancer of the oesophagus: Retrospective analyzis of three results

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Background: Oesophagectomy is the standard curative therapy for patients with clinically localized disease. The question remains concerning immediate surgical intervention or surgery after preoperative chemoradiotherapy. Many teams opt for exclusive chemoradiotherapy. The aim of this study is to analyze these three treatment alternatives.

Patients and Methods: 128 patients with localized squamous-cell oesophageal cancer (38 stage I, 71 stage IIA and 19 stage IIB according to the UICC 78 TNM classification) were treated between 1989 and 1995. They were divided into three groups: O group (treatment by oesophagectomy) n = 30, RCT + O group (treatment by preoperative chemoradiotherapy and oesophagectomy) n = 39, RCT group (treatment by exclusive chemoradiotherapy). n = 59. Factors concerning age, tumour localization and stage were similar in all groups.

Results: The O group showed no postoperative mortality, in the RCT + O group surgery mortality was 12.8%. The mortality after RCT was 1.7%. After preoperative chemoradiotherapy, oesophageal sterilization was observed in 25% of cases and the curative exeresis rate was higher (82% after RCT + O versus 60% after O). The survival difference at 5 years between the 3 groups was not significant (O group 11.6%, RCT group 21.5%, RCT + O group 42.7%). The median survival was respectively 23, 28 and 34 months. The disease free survival was identical for the O group and the RCT group. Oesophagectomy significantly improved disease free survival in patients treated by chemoradiotherapy (RCT + O versus RCT, p = 0.041). Palliative care (dilatations, prosthesis, gastrostomy or jejunostomy) to improve dysphagia was necessary in 36% of patients treated by exclusive chemoradiotherapy versus 11% of patients treated by surgery (p = 0.001).

Conclusion: Treatment by oesophagectomy or exclusive chemoradiotherapy was not significantly different. Preoperative chemoradiotherapy and surgery offered a higher survival rate than exclusive chemoradiotherapy, however, a high postoperative mortality rate was observed. This study suggests the relevance of a prospective randomized trial to compare RCT + O and RCT alone.

519 POSTER

Radio-chemotherapy and high dose rate (HDR) brachytherapy in the treatment of esophageal cancer

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Purpose: In spite of some improved results with radio-chemotherapy in locally advanced esophageal cancer local control is unsatisfactory. Because of that we increased the radiotherapy dose to the tumor with it combination of external beam radio-chemotherapy followed by HDR brachytherapy.

Methods: Our protocol consists of external radiotherapy to the esopahgus (single dose 2 Gy, total dose 56–60 Gy) and chemotherapy (5-FU 1000 mg/m^2/d, cisplatin 25 mg/m^2/d) during week 1 and 5. The percutanous radiation follow 2 HDR-brachytherapy applications, 5 Gy each/0.75 cm distance from the applicator surface.

Between Jan 92–June 98 42 pat. have been treated, median age 59 y (41–76). 34 pat received the whole treatment course; 12 pat. did not receive brachytherapy because of acute oesophagitis (5) or refusal of esophagoscopy (7). Median tumor length was 7 cm (3–12), 38/42 pat. corresponded to tumor class cT3 or cT4.

Results: 34/42 pat had endoscopically complete response. 9 pat. (8/12 pat. without and 1/30 pat with brachytherapy) developed a local recurrence after 5–20 months. Median survival was 21 months, 1- and 3- year survival rates were 74% (48%–88%) and 41% (22%–69%).

Conclusion: The combination of external beam radiochemotherapy and HDR-brachytherapy seems to improve the results concerning local control.

520 POSTER

The royal marsden experience with chemo-radiation using protracted infusional (PVI) 5-fu and cisplatin with conformal radiotherapy (CR-RT) in locally advanced oesophageal cancer

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Purpose: To establish the toxicity and efficacy, in terms of response rate and survival, to PVI 5FU, Cisplatin and Conformal RT in patients with locally advanced oesophageal cancer.

Methods: 58 patients with inoperable disease were registered for treatment with induction chemotherapy consisting of 12 weeks of PVI 5FU (300 mgs/m^2) and three weekly Cisplatin (60 mgs/m^2). RT (54 Gy) was scheduled to commence at week 12, coinciding with the final Cisplatin, and was given concomitantly with PVI 5FU (200 mgs/m^2). Response was measured symptomatically, endoscopically and by CT. Toxicity was scored by CTC, RTOG and LENT SOMA scales.

Results: Out of the 47 patients registered, 43 commenced CF chemotherapy (4 patients ineligible) and 28 (67%), went on to receive radiotherapy. Reasons for not receiving RT were; progression/death (7), Surgery (7), patient refusal (1). With induction chemotherapy, dysphagia improved in 74% of patients, CT response (CR + PR) was 51% and Gd3 + Gd4 toxicity was 17% and 7%, respectively. Overall objective response for patients completing RT was 59%. Gd 3 & 4 Oesophagitis during chemo-radiation was 24% and 8% respectively. Median survival (all patients) is 14.1 months, and 15.2 months for those completing CF RT. 1 year and 2 year survival (all patients) was 58% and 38%, respectively, and for those completing CFRT was 67% and 43%, respectively.

Conclusion: This is a well tolerated schedule producing impressive response rates, median survival and two years survival figures in a poor prognosis group of patients.

521 POSTER

First line treatment with docetaxel (D) and gemcitabine (G) in patients with inoperable pancreatic cancer: A multicenter phase II study

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Objectives: Treatment of pancreatic cancer remains disappointing. D and G have shown limited objective activity in patients with advanced pancreatic cancer but they seem to confer an improvement of disease-related symptoms. The tolerance and efficacy of their combination as 1st line treatment