3 components: pain (based on analgesic consumption and pain intensity), Karnofsky performance status, and lean body mass increase. Each parameter was measured at baseline and regularly during study. Clinical benefit was define as a sustained improvement (≥4 weeks) in at least one parameter without a worsening in any other. Following a lead-in period to characterize and stabilize pain, 126 chemonaive patients with confirmed advanced or metastatic adenocarcinoma of the pancreas (measurable or evaluable) were randomized to GEM 1000 mg/m^2 over 30 min wkly × 7 followed by 1 wk of rest, and then wkly × 3 every 4 wks thereafter, or to 5FU 600 mg/m^2 over 30 mins once wkly. Patients on both treatment arms were balanced in terms of gender, age and disease stage. CB response was the primary endpoint: 23.8% of the GEM pts were CB responders versus 4.8% of 5FU pts ($P = 0.0022$). The median survival (months) was 5.65 for GEM versus 4.41 for 5FU ($P = 0.0025$), with 24% of GEM pts and 6% of 5FU pts alive at 9 months. WHO ≥ grade 3 neutropenia was seen in 23% of GEM pts and 5% of 5FU pts, and ≥ grade 3 non-hematological toxicity (N&V, diarrhea) was seen in 15% of GEM pts and 10% of 5FU pts. This randomized study confirms the previously reported positive effect of gemcitabine on clinical benefit, and shows a survival benefit for GEM as initial treatment of patients with pancreatic cancer.

548 ORAL

PET FOR VISUALIZATION OF C-11-L-DOPA UPTAKE AND DECARBOXYLATION IN ENDOCRINE PANCREAS CANCER

M. Bergström, B. Eriksson, K. Öberg, A. Sundin, H. Ahlström, P. Bjurling, B. Långström

Uppsala University PET Centre, University Hospital, S-751 85 Uppsala, Sweden

In the old classification system endocrine pancreas tumors were described as APUDomas. This property of neuroendocrine tumors, to take up amine precursors for decarboxylation to monoamines, has been used for the diagnosis *in vivo* with positron emission tomography (PET). C-11-labelled DOPA is administered to the patients and a very high accumulation of radioactivity facilitates its identification. In two patients succeeding studies were performed with L-DOPA labelled alternatively in the β-position and in the carboxyl-group. When labelled in the β-position, the radioactivity follows the molecule to dopamine and hence a high accumulation is observed. When labelled in the carboxyl-group, the radioactivity is cleaved off as carbon-dioxide and eliminated from the tissue. This results in a low uptake in the tumor. With analysis of the kinetics, the rate of decarboxylation in the tumors is calculated.

In the same patients, examinations were performed before and after the treatment with somatostatin analogue. After treatment a 2-fold increase in the tracer accumulation is observed. This finding is explained as an indication that somatostatin analogues have minor effects on the uptake and decarboxylation process but a significant effect on release of monoamines.

549 ORAL

CAUSES OF DEATH AND RISK OF SECONDARY MALIGNANT TUMOURS IN PATIENTS WITH MALIGNANT TUMOURS OF THE SMALL BOWEL

N. Zar, J. Rastad, J. Yuen, L. Holmberg

Departments of Surgery and Cancer Epidemiology, University Hospital, S-751 85 Uppsala, Sweden

Background: There are few systematic studies of co-morbidity and risk of other cancers in patients with malignant tumours of the small bowel.

Methods: We studied 926 cases with adeno carcinoma of the small bowel and 1661 cases of carcinoid tumours reported to the Swedish Cancer Registry 1966 through 1988. Follow-up was available until 1990. The misclassification for both diagnoses was less than 5%. Standard mortality ratio (SMR) and standard incidence ratio (SIR) for second tumours were calculated.

Results: The patients with *adeno carcinoma* had increased risk to die from malignant diseases (tumours of the small bowel excluded, SMR 12.8), hematological and gastrointestinal diseases. They also had increased risk of acquiring a cancer in the female genital organs and in the gastrointestinal tract (SIR 3.5). Patients with *carcinoid tumour* showed increased risk of a tumour in the male genital organs (SIR 1.9). Standard mortality ratio was increased for endocrine disease (SMR 36.0), for cardiovascular and for gastrointestinal disease. The SMR for dying from another malignancy was 6.2).

Conclusions: Our findings support an earlier hypothesis about an association between carcinoid tumours and prostate cancer. The novel findings of associations between adeno carcinomas and risk of death in hematological disease and of carcinoid tumours and risk of dying from other, non-neoplastic endocrine disorders are relevant for further clinical investigations.

550 POSTER

GEMCITABINE IS EFFECTIVE AS PALLIATIVE THERAPY FOR 5FU-REFRACTORY PANCREAS CANCER PATIENTS

H.A. Burris III, M.L. Rothenberg, On behalf of the Multicenter Study Group

University of Texas Health Science Center, Cancer Therapy and Research Center, and Brooke Army Medical Center, San Antonio, Texas, U.S.A.

In a previous phase II trial of gemcitabine in pancreas cancer, numerous patients experienced a reduction in cancer-related symptoms and improvement in performance status. Since pancreas cancer is highly symptomatic, and therapy is difficult to assess using traditional endpoints, we designed and conducted a prospective, multicentre phase II trial with clinical benefit as the primary endpoint. Clinical benefit response was defined as a ≥50% reduction in pain (measured on a visual analogue scale), a ≥50% reduction in daily analgesic consumption, or a ≥20 point improvement in Kamofsky performance score (KPS), that was sustained for ≥4 weeks without worsening in any other component. Gemcitabine 1000 mg/m^2 (30 min infusion) was administered q wk × 7 followed by 1 wk rest, and thereafter in cycles q wk × 3 followed by a 1 wk rest. 63 pts (32 M, 31 F) with pancreatic adenocarcinoma that had progressed despite 1 prior 5-FU-based therapy were enrolled. Median age: 62 (range 33–77). Median KPS: 70 (range 50–90), median baseline pain intensity: 29 on a 100 point scale (range 3–68), median baseline analgesic requirement: 60 mg morphine-equivalents/day (range 0–1159). Therapy was very well tolerated with grade 4 toxicities reported for nausea, vomiting, neutropenia, bleeding or anaemia (each in 1 pt, 2%). Grade 3 toxicities included neutropenia (25% pts), anaemia (10%), thrombocytopenia (5%), and nausea/vomiting (6%). Under these stringent criteria, 17 of 63 pts (27%) attained a clinical benefit response (95% CI: 16–38%). We conclude that objective criteria can be used to evaluate new therapies for pancreas cancer, and that gemcitabine has substantial activity as a palliative agent.

551 POSTER

HIGH DOSE RADIOTHERAPY (RT), CONCOMITANT CHEMOTHERAPY (CT) AND HIGH DOSE RATE BRACHYTHERAPY FOR NON RESECTABLE ESOPHAGEAL CANCER

G. Calais, E. Dorval, S. Chapet, C. Berger, A. Reynaud-Bougnoux, N. Huten, L. De Calan, O. Le Floch

Centre Hospitalier Universitaire, Tours, 37044, France

RT and concomitant CT is the standard treatment for non resectable esophageal cancer. Usual total radiation dose is 50 Gy. In order to enhance local control rate a phase II study was initiated to evaluate the feasibility of a combined treatment with an external radiation dose of 60 Gy and 3 cycles of concomitant CT followed by a high dose rate brachytherapy delivering 10 Gy (2 applications with 7 days interval). 73 patients (pts), 28 men and 5 women were treated between 1989 and 1993. Stages were evaluated with CT scan and with endoscope sonography for 41 pts: 13 were Stage IIB, 50 Stage III and 10 Stage IV. Treatment consisted in a conventional fractionated RT to a total dose of 60 Gy delivered with 2 Gy per fraction, one fraction per day and 5 fractions a week. The CT regimen was a combination of Cisplatinum 25 mg/m^2 d1 to d4, 5 Fluorouracil 600 mg/m^2 continuous infusion d1 to d4. 3 cycles were administered on d1, d22 and d43. Brachytherapy was delivered one week after the end of external radiation therapy. Full radiation therapy dose was delivered for 96% of the patients. CT compliance, evaluated on the drug dose and the CT interval, was good for 77% of the patients. Overall grade 3 and 4 WHO toxicity rates were 23% and 7% respectively. One pt died from treatment toxicity. Local control rate at one year was 74%. Three-year actuarial survival rate was 27%. Distant metastase was the main cause of treatment failure. Predictive factors of late effects related to brachytherapy and evaluation of a swallowing score will be presented, In a multivariate analysis Stage was the only prognostic factor. In conclusion this regimen with high dose RT and 3 cycles of concomitant CT is feasible. Treatment results are very encouraging for pts with locally advanced disease.