p < 0.0001). Resting blood flow was elevated in PaCA in both arm (35%) and leg (72%), although peak blood flow in both arm and leg did not show any differences. The flow mediated flow was increased in PaCA by 46%.
Conclusion: Exercise capacity is significantly impaired in patients with pancreatic cancer, independent of cardiac function, and muscle blood flow. We hypothesise that symptom generation and exercise intolerance in cancer patients develop due to metabolic aberrations leading to intrinsic changes within the skeletal muscle. The pathophysiology of shortness of breath in cancer is similar to that in heart failure.

Table 1

Parameter	Patients (N = 50)	Controls (N = 40)	p-value
Peak VO_2 [mL/min/kg]	21±5.69	29.5±7.8	<0.0001
Anaerobic threshold [mL/min/kg]	12.7±3.06	15±3.27	0.003
Peak VO_2/kg lean tissue [mL/min/kg]	28.6±7.87	43.1±8.43	<0.0001
V_E/V_{CO2} slope	32.5±7.8	27.5±4.94	0.002
BMI [kg/m^2]	22.8±3.06	25.5±3.9	0.0007
Limb lean tissue mass [kg]	20.5±4.42	23.2±6.44	0.025
Lean tissue mass [kg]	49.8±9.26	51.8±12.3	0.4
Fat tissue mass [kg]	15±7.39	21.7±8.85	0.0003
LV ejection fraction [%]	60±8	62±5	0.3
MR pro-adrenomedullin [nmol/L]	0.75±0.69	0.47±0.1	0.0002
MR pro-atrial natriuretic peptide [pmol/L]	123±177	71±35	0.05
TNF receptor-1 [pg/mL]	1943±1441	1131±265	<0.0001
TNF receptor-2 [pg/mL]	2684±1413	1472±409	<0.0001
IL-6 [pg/mL]	6.9±8.7	2.0±0.9	<0.0001
Procalcitonin [ng/mL]	1.005±4.3	0.019±0.008	<0.0001
Resting blood flow arm [mL/100g·min]	6.71±3.54	4.96±1.93	0.02
Resting blood flow leg [mL/100g·min]	6.03±4.25	3.51±1.61	0.006
Flow mediated flow [mL/100g·min]	10.2±6.16	7±3.63	0.02

3529 POSTER

A phase II trial of oxaliplatin with high-dose of 5-fluorouracil and leucovorin in the first-line treatment of inoperable, locally advanced or metastatic biliary tract cancer

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Background: Advanced bile duct cancer (BTC) is a dismal disease. At the present, no standard chemotherapy is recommended. However, 5-fluorouracil (5-FU)-based is the conventional regimen in the current practice. Oxaliplatin (OXA) with 5-FU/leucorvin (LV) has approved that a better response rate and survival than 5-FU/LV in patients with metastatic colon cancer. The aim of this study was to investigate the efficacy and toxicity of OXA with 48-hour infusion of 5-FU/LV in advanced BTC as a first line and outpatient-based regimen.
Methods: Patients must have histologic confirmation carcinoma of intrahepatic, perihilar area, distal common bile duct, gallbladder and periampular vater area. Patients must have at least one measurable site of disease. Patients could not have received prior chemotherapy for advanced disease. Patients older than 20 years of age and ECOG performance status (PS) of 0−2 were included. The treatment cycle consisted with OXA (Oxalip®, TTY Biopharm Co. Ltd, Taipei, Taiwan) 85 mg/m^2 in D5W 500 ml run 2-hour premdications with dexan and 5-HT3 antagonist, followed by 48-hr infusion of 5-FU 3000 mg/m^2 and LV 100 mg/m^2 by Infusor (Baxter, USA) biweekly. The response evaluation was based on the RECIST criteria. Measurement of response was performed after every 2 months of treatment. The toxicity was assessed according to NCI common terminology criteria for adverse events version 3.
Results: From August 2005 to December 2006, 34 chemonaive patients with advanced BTC were enrolled from four sites, but two cases were not eligible for study. There were 13 females and 19 males with a median age of 62. The PS (0/1/2) was 19/11/2. The sites of disease locations included 7 intrahepatic cholangicarcinomas, 1 perihilar cancer, 10 gallbladder cancers, 5 distal common bile duct cancers, 8 ampular vater cancers and 1 unclassified location, respectively. A total of 29 patients were evaluated for response. The partial response was 6/29 (20.7%, 95% CI 8.71−40.26%), stable disease 10/29 (34.5%) and progression disease 13/29 (44.8%), respectively. The median time to progression was 116 days and the median survival was 256 days. The major Grade III/IV toxicity among 32 patients were neutropenia 6/32 (15.6%), stomatitis 3/32 (9.3%), thrombocytopenia 2/32 (6.3%), diarrhea 2/32 (6.3%), and neuropathy 1/32 (3.1%), respectively. There were no treatment-related deaths.
Conclusion: The biweekly OXA and 48-hour infusion of 5-FU/LV in patients with advanced BTC showed efficacy, tolerable toxicity and a feasible treatment for OPD-base setting.

3530 POSTER

Preliminary results from GEPTOSIS, the international study on medical treatment practice and outcomes in gastroenteropancreatic (GEP) neuroendocrine tumors (NET): variability in the time between initial diagnosis and treatment of GEP NET

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Background: There is high variability in the normal clinical practice for the treatment of GEP NET and how this may impact the clinical course of the disease is unclear. GEP NETs are generally slow-growing tumors thus treatment generally is non-aggressive. The objectives of this study are to describe treatment regimens used for newly diagnosed GEP NET patients and examine their impact on clinical outcomes, in particular outcomes associated with given doses of Octreotide LAR. Baseline characteristics and symptoms for the first 29 patients enrolled in the study are reported here.
Materials: GEPTOSIS (Neuroendocrine GEP Tumors: An Observational Study on the Impact of Sandostatin LAR) is an open label, multicenter, non-comparative, longitudinal, observational study in recently diagnosed, medically naive, functionally active GEP NET including carcinoid, insulinoma and glucagonoma. Observations include the efficacy on biochemical parameters (Chromogranin A, 5-HIAA), symptoms, and tumor volume, as well as safety and tolerability. Data are entered via a Palm-based device and transferred to a central study database. Data were collected under conditions of normal clinical practice in quarterly intervals over a period of 18 mo. It is projected that up to 276 patients will be recruited from about 100 sites world-wide.
Results: As of April 2007, 87 patients were enrolled from 38 sites worldwide; for 29 patients baseline data were available. The mean age (SD) of the patients is 58.7 yrs. (12.3); 61% are male. Diarrhea was the most common symptom at baseline (n = 18, 62%), followed by tiredness (48%), flush (45%), loss of appetite (34%), abdominal pain (21%), muscle pain (7%), vomiting and nausea (both 3%). The reported symptoms were mostly rated as moderately severe (46%), 28% were mild, 17% were severe but not incapacitating, while 9% were severe and incapacitating. The majority of patients (69%, n = 20) were enrolled in the study within 1 yr of diagnosis and 31% (n = 9) after more than 1 yr. Twenty six (90%) patients received Octreotide LAR either alone (n = 21) or in combination with surgery (n = 2), chemoembolisation (n = 1), surgery + chemoembolisation (n = 1), or radiotherapy (n = 1, for lung metastasis). 20 mg was the most common starting dose (n = 14) followed by 30 mg (n = 7) and 10 mg (n = 3).
Conclusions: Early data from GEPTOSIS indicate that diarrhea is the most common symptom at baseline. Most patients were treated with Octreotide LAR either alone or combined with other treatment. Most Octreotide LAR treated patients started with a 20 mg dose. The time between diagnosis and study entry or initiation of treatment varies considerably between patients. It has to be clarified how this might have an impact on the clinical outcome. As more data become available greater insight may be made into outcomes associated with time between diagnosis and treatment of GEP NET patients.

3531 POSTER

Toxicity and outcomes of chemoradiation without elective nodal irradiation after chemotherapy for unresectable pancreatic cancer

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Background: Optimal strategy for treating locally advanced pancreatic cancer (LAPC) is uncertain in terms of duration of chemotherapy (C) and timing of radiation (RT). This is a retrospective review to evaluate

acute toxicity and patterns of failure in patients that receive chemoradiation (CRT) for inoperable cancer of the pancreas, after non-progression on C. Conformal RT is delivered, but elective nodal irradiation is omitted.
Material and Methods: All patients received neo-adjuvant C, if tolerated at least 6 months were delivered. CRT followed this if no evidence of progressive disease was found. A dose of 45−54 Gy in 1.8 Gy/fraction was delivered with 3D conformal planning. The planning target volume (PTV) was limited to visible tumour with 1.5 cm circumferential and 2 cm cranio-caudal margin. Elective nodes were not included. Toxicities were recorded prospectively during treatment. Local progression was defined as failure within PTV and local nodes, systemic as visceral disease present. Time to progression (TTP) and overall survival (OS) are reported from the date C was started.
Results: 45 patients, M/F = 23/22; median age 61 years (range 41−83) treated between 01/1997 and 12/2006. Stage IIb = 6, III = 39; ECOG PS 0−1/2/NA = 34/6/5; CA19.9 < 100 = 24, >100 = 21. C consisted of protracted infusion 5FU modulated with other agents (PVI5FU) = 14, Capecitabine (X) = 3, Gemcitabine (G) = 13, G+X = 15. A median of 6.6 months (range 1−16.8) of C were delivered. Median dose of RT 50.4 Gy, range (23.4−54). 27 patients received C with RT (19 X, 7 PVI5FU, 1 G). RT stopped due to toxicity in 2 patients (23.4 Gy, 46.8 Gy). 6 patients had breaks in RT: 2 non-compliance (4 days), 4 due to toxicity (2−28 days). During CRT 13 (28.8%) patients had grade 3 toxicities, 9 (20%) patients GI toxicity: (nausea = 6, vomiting = 2, diarrhoea = 1); fatigue = 2, abdominal pain due to tumour = 3, sepsis = 4, skin = 2, other = 3. One patient had grade 4 vomiting and 1 patient died shortly after RT due to perforated duodenal ulcer in RT field. 5 had C stopped or dose reduction during RT. The first site of failure was local in 8 patients, local and systemic in 6 and systemic in 22 patients. Median TTP was 13.5 mo; median survival 19.7 mo, 1-year OS = 79%, 2-yr OS = 28%.
Conclusion: Sequential C then CRT shows promising efficacy in the treatment of LAPC in a highly selected group of patients. The low proportion of local failures indicates that prophylactic nodal irradiation could be omitted to facilitate delivery of CRT.

3532 POSTER

Histopathological response to preoperative chemoradiation for resectable pancreatic adenocarcinoma: the French phase II FFCD 9704-SFRO trial

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Background: To define and evaluate histopathological response rates with preoperative chemoradiation (RT-CT) for resectable pancreatic adenocarcinoma.
Materials and Methods: Forty-one patients (pts) with localized, potentially resectable pancreatic adenocarcinoma were treated with 50 Gy combined with 5-Fluorouracil (300 mg/m^2 /d; d1-d5; week 1−5) and Cisplatin (20 mg/m^2/d; d1-d5 and d29-d33). Radiographic restaging was performed 4 to 6 weeks later and pts presenting with resectable disease underwent surgical resection.
Results: Twenty-six (63%) of 41 pts underwent curative surgery. Standardized histologic response was measured and graded by a single pathologist. The effectiveness of the preoperative chemoradiation was defined by the proportion of severly degenerative cancer cells (SDCC), their density and histological distribution and the proportion of necrotic tumoral tissue. Eleven of 24 (46%) specimens presented more than 80% of SDCC, and 8/11 (72%) specimens were associated with large necrosis areas. The histologic distribution was characterized by the low density of nonaffected cancer cells, and an important fibrous and amorphous connective tissue associated with cancer-cells' defects (type A of the Ishikawa's classification). Histologic complete response was observed in one specimen, and 9/24 (37%) specimens were characterized by 50 to 80% of SDCC. Finally, 4/24 specimens presented with a low rate of SDCC, few necrosis area and several non affected cancer cells (Ishikawa C).
Conclusion: Preoperative 5-Fluorouracil-Cisplatin-based concurrent RT-CT for resectable pancreatic adenocarcinoma provides antitumoral effect. With regard to the feasibility of this therapeutic schedule and the rate of major histologic response, this approach could offer a clinical benefit. Further gemcitabine-based chemoradiation regimens, will determine the predictive factors of the treatment response, and the improvement in survival. This study is the first in Europe to present histopathological data on a prospective approach.

3533 POSTER

Cetuximab plus Gemcitabine/Oxaliplatin (GEMOXCET) in 1st line metastatic pancreatic cancer – a multicenter phase II study

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Background: Targeting the epidermal growth factor receptor (EGFR) pathway in pancreatic cancer seems to be an attractive therapeutic approach. The present study assessed for the first time the efficacy of cetuximab plus the combination of gemcitabine/oxaliplatin in metastatic pancreatic cancer.
Methods: Eligible subjects had histological or cytological diagnosis of metastatic pancreatic adenocarcinoma. The primary endpoint was response according to RECIST. Patients (pts) received cetuximab 400 mg/m^2 at first infusion followed by weekly 250 mg/m^2 combined with gemcitabine 1000 mg/m^2 as a 100-minute infusion on day 1 and oxaliplatin 100 mg/m^2 as a 2-hour infusion on day 2 every 2 weeks.
Results: Between January 2005 and August 2006 a total of 64 pts [22 women (34%), 42 men (66%); median age 64 years (range 31−78)] were enrolled at 7 study centers. At April 2007 a total of 37 pts are still alive. 58 pts are evaluable for baseline and toxicity analysis. 6 pts had no treatment or an incomplete drug combination within the first cycle of the treatment plan (n = 3 hypersensitivity reactions to the first cetuximab infusion, n = 1 rapid tumor progression, n = 2 lost of follow-up). Reported grade 3/4 toxicities (% pts) were: leucopenia 12%, anemia 16%, thrombocytopenia 11%, diarrhea 7%, nausea 14%, infection 19%, allergy 4%. Cetuximab-attributable skin reactions occurred as follows: grade 0: 28%, grade 1: 43%, grade 2: 22%, grade 3: 7%. The intention-to-treat analysis of 50 evaluable pts shows an overall response rate of 32% including 1 (2%) complete and 15 (30%) partial remissions. There were 30% pts with stable and 38% pts with progressive diseases or interruption of the therapy. Median time to progression is 123 days with a preliminary overall survival estimation of 8 month. A clinical benefit response was noted in 23 of evaluable 54 pts (43%).
Conclusion: The addition of cetuximab to the combination of gemcitabine and oxaliplatin is well tolerated and exhibits a high response rate. Further evaluation in a phase III trial is warranted.

3534 POSTER

Patients with ERCC1-negative tumors may benefit from preoperative CRT in resectable esophageal cancer

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Background: We reported that preoperative chemoradiotherapy (CRT) did not show survival advantage to surgery alone in general patients with resectable esophageal cancer (Lee JL et al., Ann Oncol 2004;15:947−54). We investigated the effects of preoperative CRT on survival according to ERCC1 status in resectable esophageal cancer.
Materials and Methods: Paraffin-embedded pretreatment tumor specimens, collected by endoscopic biopsy from patients treated either with surgery alone or with preoperative CRT (5-FU/cisplatin or capecitabine/cisplatin with 46.5−48 Gy of radiation) followed by surgery, were analyzed by immunohistochemical assay for ERCC1. Staining intensity and proportion of ERCC1 were graded on a scale of 0 to 3, and the resulting scores were multiplied to obtain a semiquantitative score (0−9).
Results: Between March 1993 and June 2005, 175 patients were treated with preoperative CRT followed by surgery or surgery alone as part of prospective clinical trials. Of those, 152 biopsy specimens (111 in the