Results: Of 283 patients reviewed, 173 (61.1%) patients had oesophageal cancer while the remaining had gastric carcinoma. TED was detected in 31 (10.9%) patients overall. The incidence of TED was the same in both oesophageal and gastric cancer patients. TED was: PE 10, DVT 15 (9 related to indwelling venous catheter), IHD 3 and CVA 3. 19.3% of patients with TED presented with clinically occult TED (3 DVT and 3 PE) detected on imaging. All patients who developed TED received platinum-based chemotherapy and this accounts for 12% of patients who received platinum-based chemotherapy for the above period. None of the 4 patients who received irinotecan combination chemotherapy developed TED. 64.5% of patients were subsequently hospitalised following TED diagnosis with no TED-specific mortality.
Conclusions: Our observations suggest TED is a frequent complication of chemotherapy for gastroesophageal cancer patients. The majority of patients are symptomatic, however with improved imaging technology such as use of multidetector CT scanning occult TED may increasingly be detected. The potential use of antiangiogenic agents with conventional cytotoxic chemotherapy may increase the incidence further. If these observations are confirmed in larger prospective cohort studies, thromboprophylaxis may be justified, however may be difficult due to the risk of GI bleeding in these patients.

3523 POSTER

Glufosfamide (GLU) plus gemcitabine (GEM) in pancreatic adenocarcinoma: results of a Phase 2 trial

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Background: Glufosfamide is glucose linked to isophosphoramide mustard, the active metabolite of ifosfamide. Cancer cells use glucose at a higher rate than normal cells, which may lead to preferential metabolic targeting by GLU. The Phase 1 study established a GLU dose of 4500 mg/m^2 for the GLU + GEM regimen. The objectives of the Phase 2 part of this study were to evaluate the safety and efficacy of GLU+GEM in pts with pancreatic adenocarcinoma.
Materials and Methods: Eligible pts had metastatic and/or locally advanced pancreatic adenocarcinoma previously untreated with chemotherapy, Karnofsky Performance Status $\geqslant$70, creatinine clearance (CrCL) $\geqslant$60 mL/min and acceptable hematologic and liver function. Pts received GLU 4500 mg/m^2 iv over 4 hours on Day 1 and GEM 1000 mg/m^2 iv over 30 minutes on Days 1, 8 and 15 of every 28-day cycle. CT scans were done every 8 weeks. Primary endpoint was response rate.
Results: Twenty-nine pts were enrolled. One patient with ineligible histology was excluded from efficacy analyses. The 14 male/15 female pts had a median age of 59 years. Twenty-three pts had distant metastases; 6 pts had locally advanced disease. Median cycles on treatment was 4 (range 1−14+). Eight pts completed all 6 cycles including 5 pts with stable or responding disease who continued on study for additional cycles. Six of 28 (21%; 95% CI: 8−41%) pts had a partial response (duration 1.0+ to 9.7+ months) one unconfirmed. Eleven of 28 (39%) pts had stable disease (median duration 5.3 months). Median progression-free and overall survival were 3.7 and 6.0 months. Six-month survival was 50% (95% CI: 35−72%). Grade 3 and 4 neutropenia occurred in 9 (31%) and 13 (45%) pts. Grade 3 and 4 thrombocytopenia occurred in 7 (24%) and 1 (3%) pts. Five pts (18%) had a GLU-related serious adverse event (SAE); renal tubular acidosis (RTA) with renal failure (2 pts), RTA, vomiting, nausea. Three pts died from SAE unrelated to GLU. Another pt developed renal failure after hypotension associated with pulmonary embolus. The CrCL fell below 60 mL/min in 10 of 27 (37%) pts with CrCL $\geqslant$ 60 at baseline. Median change in CrCL from baseline to last measurement was −6 mL/min.
Conclusions: These data indicate that GLU + GEM may benefit pts with chemotherapy naive pancreatic adenocarcinoma. Hematologic and renal toxicity may be more than would be expected with either agent alone. No unanticipated adverse events based on previous experience with glufosfamide were observed.

3524 POSTER

High rate of clinical benefit response in patients with advanced biliary tract cancer receiving gemcitabine plus capecitabine. A prospective, multicenter phase II trial of the Swiss Group for Clinical Cancer Research (SAKK 44/02)

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Background: In phase II trials, several chemotherapy regimens have yielded tumor response rates of 20−30% with survival times between 7−12 months in patients (pts) with advanced biliary tract cancer. However, no information is available on patient-reported outcomes in this group. As primary objective we evaluated the association of palliative chemotherapy with tumor-related symptoms measured using clinical benefit response parameters [Burris et al., J Clin Oncol 1997].
Materials and Methods: Previously untreated pts with pathologically confirmed, locally advanced, unresectable or metastatic biliary tract cancer were recruited. Pts had to be symptomatic of biliary tract cancer and have at least one of the following at baseline: Karnofsky performance status (KPS) between 60 and 80, and/or average baseline analgesic consumption $\geqslant$10 mg morphine equivalents per day, and/or average pain intensity score of $\geqslant$20 mm (based on a visual-analogue scale). Treatment consisted of gemcitabine 1 g/m^2 IV on days 1 & 8 with capecitabine 650 mg/m^2 orally BID on days 1−14 of a 3 week cycle for a maximum of 8 cycles. The primary endpoint was the number of pts categorized as clinical benefit responders (CBR) or stable CBR (SCBR) on all of the clinical benefit parameters (pain intensity, analgesic consumption, KPS and weight) determined on the basis of the first 3 cycles. Secondary endpoints were clinical benefit rate in all cycles, tumor response (RECIST), adverse events, quality of life, time to progression (TTP) and overall survival (OS).
Results: Between May 2003 and June 2006, 44 pts were enrolled (8 with gallbladder cancers, 36 with bile duct cancer) in 6 centers. Median age was 65 years. A total of 266 cycles were administered (median 8) with an overall relative dose intensity of 90%. Main grade 3/4 adverse events included: neutropenia (39%), anemia (2%), thrombocytopenia (7%), fatigue (11%), nausea (5%), constipation (5%), vomiting (2%) and diarrhea (2%). After 3 cycles, 16 pts (36%) achieved a CBR and 15 pts (34%) achieved a SCBR. Over the full course of treatment, 25 pts (57%) achieved a CBR and 8 pts (18%) a SCBR. We observed 1 CR (2%), 10 PRs (23%) and 24 SDs (55%). Median TTP and OS were 7.2 months and 14.2 months, respectively.
Conclusions: Combination chemotherapy with gemcitabine plus capecitabine is well tolerated, effective and leads to a high number of CBR. CBR can be used to evaluate the impact of palliative chemotherapies in pts with biliary cancer.

3525 POSTER

Low dose sequential multi-drug regimens for the elderly and the resistant advanced pancreatic cancer patients.

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Background: The GFLIP regimen was designed based on human ex vivo sensitivity tests performed on a series of de novo pancreatic tumors, which identifed multiple drug interactions optimum at low drug concentrations. The regimen provides conditions for these drug interactions to occur simultaneously and overcome the individual tumors heterogeneous resistance to many drug combinations.
Methods: Pts with unresectable, metastatic and recurrent pancreatic cancer were treated with a low dose q2wk version of GFLIP using cisplatin 40 mg/m^2 with or without subsequent addition of low dose docetaxel 25−35 mg/m^2 on failure of GFLIP. Pts with PS 4, atypical cystic pathology, apocrine or endocrine tumors and Ro staus were excluded from analyses. Eligibility allowed prior treatment with the test drugs. Cohorts of consecutively accrued pts provided 185 prospectively registered pts for intent to treat analyses of overall survival, plus age, stage, prior therapy and

sex as prognostic factors. An additional analysis omitted all pts surviving 2 years or more.
Results: The distribution of patients characteristics was Stage IV 66%, Stage II-III 34%; prior therapy: 30%; age: 106 over 65, 44 over 75, 14 over 80; sex: 94 male. Overall median survival was 16.4 mos (14.7−18.1 mos). Overall one year survival was 62% two year survival was 29% and three year survival was 21%. Age greater that 65, 75 and 80 were not adverse prognostic factors for treatment p: 0.69−0.82. Prior treatment was not an adverse prognostic factor. Analyses found no significant differences in the distribution of patient chararcteristic within the subsets of patient of all ages and treatment histories. Analyses excluded pts survivng 2 years or more found a median survival of 12.5 (9.6−15.5) mos. There were no treatment related deaths nor unanticipated toxicities. Hospitlizations for treatment related adverse events including crossover regimen occur in less than 1% of cycles. The limiting toxicity of GFLIP is late mild-moderate neurotoxicity and on adding docetaxel brief moderate/severe cytopenia and fatigue.
Conclusion: Low dose GFLIP followed by GFLIP/docetaxel is safe and offers survival benifit for the majority of pts including bioth the elderly, the previously treated, and the poor risk as suggested by analyses omitting 2 year survivors.

3526 POSTER

Prognostic value of carbohydrate antigen (CA)19−9 decrease in response to chemotherapy for advanced pancreatic adenocarcinoma (PA)

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The assessment of chemotherapy (CHT) activity in PA is hampered by fibrotic and desmoplastic reactions. A decrease of basal CA19−9 level >49% during CHT predicts better survival (OS). This study was aimed to determine whether a different cut-off level of basal CA 19−9 decrease may allow to better assess response to CHT. Between April '97 and January '07, 251 chemo-naive patients with stage III (N = 88; 35%) or metastatic (N = 163; 65%) citologically proven PA were enrolled in 5 trials at our institution to receive either gemcitabine alone (gem; N = 32) or 4-drug gem-based combination (4D; N = 219). Response to CHT was assessed by bimonthly CT scan while CA19−9 was detected on a monthly basis. Median (m) and 1y OS was 10 months and 39%. OS per response group is reported in table 1. The differences among OS curves were significant (progressive disease [PD] vs stable disease [SD] $p < 0.00001$; PD vs partial response [PR] $p < 0.00001$; SD vs PR $p = 0.0007$). Baseline CA19−9 was detected in 248 patients (99%) and was elevated in 210 (84%). In 190 of 210 patients (90%) CA19−9 variation during CHT was available. OS per CA19−9 response group is reported in table 1. OS for group D was significantly better than for other groups (D vs B $p = 0.0004$; D vs C $p = 0.0004$; D vs A $p < 0.00001$). No difference was observed between groups B and C ($p = 0.14$) and A and B ($p = 0.18$), while group C had better OS than group A ($p = 0.006$). Based on these results we recommend to use the rate of patients with basal CA19−9 decrease >89% as a complementary measure of outcome when assessing CHT activity against PA.

Table 1.

Response	Number	mOS	1y OS
PD	66 (26%; gem 69%; 4D 20%)	4.5	8%
SD	74 (29%; gem 22%; 4D 31%)	10.2	34%
PR	111 (44%; gem 9%; 4D 49%)	15.0	60%
↓ CA19.9 <50% group A	61 (32%; gem 50%; 4D 29%)	7.4	18%
↓ CA19.9 50−69% group B	23 (12%; gem 19%; 4D 11%)	9.5	26%
↓ CA19.9 70−89% group C	50 (26%; gem 23%; 4D 27%)	10.0	36%
↓ CA19.9 >89% group D	56 (30%; gem 8%; 4D 33%)	16.6	74%

3527 POSTER

Outcome of the non randomized patients in the FFCD 9102 trial: chemo-radiation followed by surgery compared with chemo-radiation alone in squamous cancer of the esophagus

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Background: for locally advanced thoracic oesophageal cancers, the FFCD 9102 trial have demonstrated that for responders chemo-radiation only was equivalent to chemo-radiation followed by surgery in terms of overall survival [1]. What about non randomized patients?
Materials and Methods: out of 451 patients, 192 were not randomized because of no objective response or improved dysphagia, contraindication to either surgery or continuation of chemo-radiation, patient's refusal, death or no further treatment.
Results: at the end of the induction chemo-radiation, there was no difference between randomized and non-randomized patients in term of age, tumor height and diameter, doses of chemotherapy or radiotherapy. However, weight loss, body surface and Spitzer QoL Index were significantly different. Duration of follow-up was identical: 47.3 months vs 48.1 months (NS). Overall survival was significantly lower in non-randomized patients: median survival 11.5 months (SE = 1.09 months) vs 18.9 months (SE = 1.03 months) in randomized patients (HR = 1.40 [95% CI, 1.13 to 1.74], $p = 0.0024$). In the non-randomized group 112 patients were operated on, among them 80 had R0 resection (42%). For all patients operated on median survival was 17.3 months (SE = 0.65 months) versus 6.1 months (SE = 0.46 months) in non-operated patients ($p < .0001$), and was not different from survival of the randomized ones ($p = 0.58$).
Conclusion: surgery is a valuable option for patients non responding to a planned exclusive chemo-radiation therapy.

References

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3528 POSTER

Fatigue in pancreatic cancer: the potential link between exertional dyspnea, exercise limitation, skeletal musculature and neurohormonal activation

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Background: In cancer, dyspnea and reduced exercise capacity are frequently seen, but their origin is unclear. We suggest, the symptoms are due to metabolic changes within the skeletal musculature as has previously been shown for patients with heart failure.
Methods: We examined 50 patients with pancreatic cancer (PaCA, age 60±10 years [mean±SD], 20 female). Symptom limited exercise capacity (treadmill), body composition (DEXA), left ventricular (LV) systolic and diastolic function (echocardiography) and limb post-ischemic peak blood flow (i.e. muscle perfusion) were assessed. 40 healthy subjects served as controls (age 57±10 years, 19 female).
Results: 49% of PaCA patients were classified as NYHA class II or III. In PaCA patients, exercise capacity (peak VO2) was reduced by 30%, anaerobic threshold by 13% and peak VO2/kg lean tissue by 33%, while VE/VCO2-slope as a measure of ventilatory inefficiency was increased by 14% (table 1). Compared to controls, patients with PaCA had reduced limb lean mass (9%), lower fat tissue mass (32%). Total peak VO2 closely related to limb lean mass in controls ($r = 0.81$, $p < 0.0001$), but much less in PaCA ($r = 0.42$, $p = 0.004$). LV ejection fraction and diastolic function (E/A, E/e′) were normal and not different between groups. Markers of cardiovascular neurohormonal activation like mid-regional (MR) pro-adrenomedullin (60%) and MR pro-ANP (73%) as well as markers of inflammation (sTNFRs, procalcitonin) were increased in PaCA patients (all