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