preoperative CRT [CRT-S] group and 41 in the surgery alone [S] group) were available for immunohistochemical analysis. ERCC1 expression were classified into positive (score >4) and negative (score⩽4) based on median value of ERCC1 expression. Patients and disease characteristics were comparable between 2 groups. ERCC1 expression was positive in 71 patients (47%). With a median follow-up of 44 months, median overall survival (OS) of surviving patients was 45.6 months in the S group and 47.8 months in the CRT-S group, and median event free survival (EFS) was 36.7 months in the S group and 38.4 months in the CRT-S group. Neither EFS nor OS differed between groups (p = 0.763 and 0.462, respectively). However, among patients with ERCC1-negative tumors, those who received preoperative CRT had longer OS and EFS compared with those treated with esophagectomy alone (median OS; 59.2 months vs 29.4 months, p = 0.0568, median EFS; 50.7 months vs 19.7 months, p = 0.0415) but not among patients with ERCC1-positive tumors (p = 0.304 and 0.516, respectively). Among patients who received esophagectomy alone, those with ERCC1-positive tumors had a tendency toward longer OS and EFS compared to those with ERCC1-negative tumors (p = 0.085 and 0.094, respectively).
Conclusions: Patients with ERCC1-negative tumors may benefit from preoperative CRT compared with surgery alone in resectable esophageal cancer.

3535 POSTER

Phase II trial investigating the efficacy and safety of sunitinib in patients with unresectable hepatocellular carcinoma (HCC)

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Background: The oral multitargeted tyrosine kinase inhibitor, sunitinib malate (SUTENT®; SU), has demonstrable antitumour activity and is approved for the treatment of advanced RCC and imatinib-resistant or intolerant GIST. The tyrosine kinases VEGFR and PDGFR, which play key roles in HCC proliferation and tumour angiogenesis, are targets for SU. In this phase II, open-label, single-agent study, we investigate the efficacy and safety of SU in European/Asian patients (pts) with unresectable HCC.
Patients and Methods: Pt eligibility criteria included histologically confirmed HCC, ECOG PS ⩽ 1, CP score −A/−B, adequate organ function and no brain metastases, clinically relevant ascites or prior liver transplant. Pts received SU 50 mg/day for 4 wks, every 6 wks (4/2 schedule). The primary endpoint was ORR measured by RECIST. Other endpoints included time-to-event rates, safety (NCI CTCAE v3.0), PK and other measures of antitumour activity (tumour density, volumetric measurement of percent tumour necrosis [VMTN] and intra-tumour blood perfusion by CT scan).
Results: Baseline pt characteristics were: n = 37; median age=61 yrs, range 29–82; male=92%; PS 0:1, 51%:49%; CP −A/-B, 84%/16%; 40.5% with prior local treatments. Pts received a median of 2 SU cycles (range 1–8). RECIST assessment indicated one partial response and 35% with stable disease. Median overall survival was estimated to be 45 wks (range 22.0–not reached). Grade 1/2 skin toxicity was common. Grade 3/4 toxicities included thrombocytopenia (35%), neutropenia (24%), CNS symptoms (22%), asthenia (22%) and haemorrhage (22%). Grade 5 events included bleeding, drowsiness, hepatic encephalopathy and renal failure (n = 4). 43% of pts required at least one SU dose reduction. There were no differences in drug exposure between CP-A and −B groups. Tumour density decreased in 68% of pts. Major (>50%) and minor (<50%) post-treatment tumour necrosis, measured by VMTN, occurred in 46% and 25% of pts, respectively. A 39% decrease (range 13–72%) in post-treatment tumour blood perfusion parameters (blood volume and flow) occurred.
Conclusions: Major tumour necrosis was observed in almost half of pts in this study following SU treatment, suggesting potent antitumour activity of SU in unresectable HCC. Change in tumour size may not be the most appropriate endpoint for assessing SU efficacy in HCC pts. These findings, which are consistent across European and Asian pts, warrant further investigation of SU in this pt population.

3536 POSTER

A phase II study of induction chemotherapy with gemcitabine plus S-1 (GS) followed by chemoradiation for locally advanced pancreatic cancer (LAPC)

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Background: Most patients (pts) with LAPC treated by chemoradiation (CRT) eventually develop metastasis progression. Thus, effective systemic chemotherapy is required, even for pts with LAPC. Gemcitabine plus S-1 (GS) chemotherapy has been shown to yield a high tumor response rate in cases of advanced pancreatic cancer. Here, we conducted an early phase II study to examine the efficacy of GS therapy followed by CRT in pts with LAPC.
Methods: The eligibility criteria for enrolment in the trial were: histologically proven LAPC, age >20 years, performance status (PS) of 0 or 1, and no history of prior therapy. The pts received 4 cycles of induction GS chemotherapy (gemcitabine, 1000 mg/m^2, days 1, 8; S-1, 40 mg/m^2 bid, days 1−14; every 21 days). Subsequently, pts who did not show progression received CRT (30 Gy, 10 fractions, 2 weeks; gemcitabine, 250 mg/m^2, days 1, 8). After the CRT, at least 2 cycles of standard gemcitabine (1000 mg/m^2, days 1, 8, 15; every 28 days) were administered. The primary endpoint of the study was the progression-free survival (PFS) rate at 6 months. A PFS of 50% at 6 months was expected in this trial.
Results: Between February 2005 and October 2006, 20 pts (median age: 63.5 years [33−75 years], PS 0/1: 15/5, male/female: 10/10) were enrolled. The induction GS chemotherapy was completed in 18 pts. Two pts showed disease progression (general deterioration) during the induction GS chemotherapy. Grade 3/4 hematological toxicities were observed in 13 pts (65%), and grade 3 febrile neutropenia was observed in 1 patient. Grade 3 non-hematological toxicities were observed in 5 pts (nausea and anorexia were the most common). Dose reduction was necessitated in 5 pts (25%). Two pts showed disease progression after completion of the induction GS chemotherapy. Subsequently, 16 pts received CRT, which was completed without delay in all. Grade 3 hematological toxicities were observed in 2 of these 16 pts. Five (25%) partial response were observed among all evaluable pts. Laparotomy with curative intent was undertaken in 4 pts, and R0 resection could be accomplished in 3. A pathological complete response was observed in 1 of these patients. The PFS rate at 6 months was 70% (14/20, 95% CI: 45.7−88.1%). The median overall survival period was 11.0 months (95% CI: 5.4−16.5 months).
Conclusions: Induction GS chemotherapy followed by CRT is a feasible and promising strategy for the treatment of LAPC. A multicenter trial on a larger sample size is warranted to confirm the efficacy and survival benefit of this treatment observed in this study in patients with LAPC.

3537 POSTER

Variations in KIT and PDGFRA mutations in gastrointestinal stromal tumours

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Gastrointestinal stromal tumors (GISTs) are characterized with oncogenic mutations, leading to constitutive, ligand independent activation of KIT tyrosine kinase. KIT (CD117) appeared to be an extremely helpful marker in discriminating GISTs from other mesenchymal tumors. In GISTs with wild-type KIT protein the mutations in PDGFRA gene were shown. To determine the KIT and PDGRFA mutations in GISTs and estimate their prognostic value, we analyzed 68 genomic DNA extracted from paraffin sections. DNA was amplified with primers to exons 11, 9, 13, 17 of KIT and exon 18 of PDGRFA followed with direct sequencing. Seventy three percents of GISTs harbor KIT mutations in exon 11, namely, 74% of gastric tumors, 63% of intestinal tumors and 100% of GISTs of rectum. The most frequent mutations were in-frame deletions in the region of 550–563aa at the 5′-end of KIT exon 11. The point mutations were localized in 557, 559 and 560 codons. GISTs with KIT mutations that targeted to 557, 558