or 559aa in the 5′-end of exon 11 were low differentiated tumors with recurrences or metastases. There was one gastric GIST with the deletion of 550–558aa that started in KIT intron 10 and involved the intron 10 – exon 11 boundary. There were rather frequent mutations in the 3′-end of KIT exon 11: 20% of GISTs demonstrated in-frame deletions or duplications of 1−12 aminoacid residues in the region of 569–586aa of KIT. Insertions in the 3′-end of KIT exon 11 were found predominantly in GISTs of low malignancy in women over age 65. KIT mutations in exon 9 (duplications of 502–503aa) were detected in 26% of intestinal GISTs. There was one gastric GIST with mutation in KIT exon 17. PDGRFA mutations in exon 18 were found in 8% of GISTs. Substitution D842V was found only in one benign gastric GIST with epithelioid cell morphology. The other PDGRFA mutations were size-altering deletions, involving 842–846aa. There were five GISTs with wild-type KIT and PDGFRA. The obtained results revealed some correlations between the type of KIT and PDGRFA mutations and clinicopathologic parameters of GISTs. They support the suggestion that mutation analysis may be used as additional parameter for predicting GISTs prognosis and response to target-affective therapy.

3538 POSTER

Phase I study of concurrent chemoradiation including twice-weekly low dose gemcitabine for unresectable pancreatic adenocarcinoma

F. Mornex[1], M. Ychou[2], C. Mercier[3], B. Chauffert[4], A. Serres[1], V. Wautot[1], A. Kubas[1], N. Girard[1], P. Roy[3]. *[1]Centre Hospitalier Lyon Sud, Radiation Oncology, Lyon Pierre Benite, France; [2]Centre Val D'aurelle, Medical Oncology, Montpellier, France; [3]Centre Hospitalier Lyon Sud, Biostactistics, Lyon Pierre Benite, France; [4]Centre Georges Francois Leclerc, Medical Oncology, Dijon, France*

Background: To determine the maximum tolerated dose (MTD) and dose-limiting toxicities, as well as potential antitumor activity of twice-weekly gemcitabine and concurrent irradiation in patients presenting with unresectable locally advanced, or metastatic and painful pancreatic adenocarcinoma.
Materials and Methods: Thirty six patients with histologically proven adenocarcinoma of the pancreas have been treated in Centre Hospitalier Lyon Sud, France, between 2000 and 2005. The initial dose of gemcitabine was 30 mg/m^2 by 30-minute intravenous infusion twice a week, for 5 consecutive weeks concurrent with 50 Gy of radiation within 5 weeks, delivered to the pancreatic area. Gemcitabine doses were escalated in 10 mg/m^2 increments in successive cohorts of three to six patients until dose-limiting toxicities were observed. A limiting toxicity is defined as a grade 4 or 5 toxicity.
Results: Thirty six patients have been included, mean age 57 years old (38−73), 25 male and 11 female, all evaluable. Concurrent radiation and twice-weekly gemcitabine at 30-, 40-, 50-, 60-, 70 mg/m^2 were well tolerated, without limiting toxicities observed. All patients received the full dose of radiation, and 16/24 (67%) patients received at least 70% of the prescribed dose. At level 80 mg/m^2 twice a week, 2/6 limiting toxicities have been observed: radiation-induced Gr. 4 gastric ulcer with vomiting and radiation-induced Gr.4 eso-gastritis. At this level, all patients received the full dose of radiation, and the mean gemcitabine delivered dose was 616 mg/m^2, i.e. 77% of the prescribed dose. The MTD for twice-weekly gemcitabine is 80 mg/m^2, the recommended dose 70 mg/m^2.
Conclusions: Definitive results will be presented for the first time, with a recommended dose 70 mg/m^2 when twice-weekly Gemcitabine and radiation are delivered. The complete cohort of patients will be finally analyzed for toxicity, survival and relapse patterns. The next phase I trial will include new agents in addition to gemcitabine and radiation, for the same type of patients.

3539 POSTER

High-dose 3D-Conformal Radiation Therapy (CRT): a new curative treatment for patients with small hepatocellular carcinomas (HCC). Mature results of a French phase II trial (RTF1)

F. Mornex[1], V. Wautot[1], A. Kubas[1], A. Serres[1], E. Maillard[1], C. Trepo[2], P. Merle[2]. *[1]Centre Hospitalier Lyon Sud, Radiation Oncology, Lyon Pierre Benite, France; [2]Hôpital Hotel Dieu, Hepatogastroenterology, Lyon, France*

The aim of this phase 2 trial was to evaluate the tolerance and efficacy of high-dose conformal radiotherapy (CRT) for small size HCC developed in cirrhotic liver and non suitable for curative therapies.
Background: Small size HCC benefit from curative therapies (liver transplantation, surgical resection or percutaneous destruction) while others are candidates for palliative options. Although liver conventional external radiation is regarded as little efficient and potentially toxic in cirrhotic patients (pts), 3D-conformal radiotherapy (CRT) for single HCC nodules demonstrated recent promising results.
Materials and Methods: A prospective phase 2 was conducted in 26 pts with small HCC (1 nodule $\leqslant$5 cm, or 2 nodules $\leqslant$3 cm) not suitable for curative treatment, Child-Pugh class A (15), B (8), 19 males, mean age 70, mean tumor size 3.2 cm. The aim was to assess the tolerance and efficacy of CRT (primary endpoint: rate of complete tumor response assessed by contrast-enhanced spiral CT scan showing disappearance of the arterial contrast enhancement on 2 successive examinations at 3 mo interval; secondary endpoint: toxicity assessment, using NCI then RTOG-EORTC Soma-Lent grading scales). CRT delivered 66 Gy (2 Gy/fraction, beam energy >10 MV). Tolerance was evaluated by using dose-volume histograms and normal tissue complication probability.
Results: Out of the 23 currently evaluable pts, 18 (78%) achieved a complete tumor response, maintained with time, and 5/23 no response (potential residual hypervascularisation but unchanged size of tumor). With a median follow-up of 17$\pm$8 mo, 2 pts relapsed on the irradiated tumor bed at 12 and 30 mo. No grade 4 toxicity was observed in 16 Child-Pugh A pts. Gr. 4 biochemical toxicity was observed in 2/9 pts Child-Pugh B (thrombocytopenia, hyperbilirubinemia), gr. 3 in 4 pts, 1 developed a gr. 3 portal hypertensive bleeding requiring transfusion, 1 pt a jaundice with edema and ascites at 1 mo, which spontaneously resolved.
Conclusion: This phase II trial showed for the first time in Europe that High Dose CRT can induce a complete tumor response maintained with time (local control) in 78% of pts presenting with small HCC nodules. Tolerance seemed to be better in Child-Pugh A pts than Child-Pugh B. This non invasive technique is highly suitable for tumors unreachable by percutaneous destruction. The current study (RTF2) evaluates the tolerance and efficacy of chemoembolisation followed by radiation for large lesions (>5 cm).

3540 POSTER

Postoperative adjuvant gemcitabine plus oxaliplatin (GemOx) chemotherapy followed by chemoradiation in patients with pancreatic carcinoma: mature results of a multicenter phase II study

F. Mornex[1], T. Andre[2], C. Louvet[3], J.F. Seitz[4], M. Ychou[5], G. Lledo[6], J. Balosso[7], C. Partensky[8]. *[1]Centre Hospitalier Lyon Sud, Radiation Oncology, Lyon Pierre Benite, France; [2]Centre Hospitalier Tenon, Medical Oncology, Paris, France; [3]Hôpital Saint Antoine, Medical Oncology, Paris, France; [4]Hôpital Saint Antoine, Hepatogastroenterology, Marseille, France; [5]Centre Val D'aurelle, Medical Oncology, Montpellier, France; [6]Clinique Saint Jean, Medical Oncology, Lyon, France; [7]Centre Hospitalo-Universitaire, Radiation Oncology, Grenoble, France; [8]Hôpital Edouard Herriot, Digestive Surgery, Lyon, France*

The primary objective of this multicenter phase II non randomized study is to evaluate the overall survival rate, recurrence free 1-year survival rate, the time to disease progression and local recurrence rate for patients who have benefited from potentially curative surgery for pancreatic cancer, followed by an adjuvant chemoradiation regimen.
Background: Gemcitabine (Gem) has potential activity in advanced pancreatic cancer and is a powerful radiosensitizer. We evaluated the potential effectiveness and feasibility of postoperative GemOx chemotherapy followed by concurrent Gem and irradiation (RT) after curative resection for pancreatic adenocarcinoma.
Materials and Methods: Fifty-four patients with resected adenocarcinoma of the pancreas and negative resection margins (R0) were entered. Gem 1000 mg/m^2 over 100min on d1 then Ox 100 mg/m^2 (120min) on d2 were given (q2w for 6 cycles). After a 4-week rest period, Gem 100 mg/m^2 weekly combined with RT 50 Gy (2 Gy/fraction) were administered over 5 weeks in patients with no residual toxicity and no recurrence. Only patients who underwent both regimens are followed up to 24 months.
Results: The treated population (at least 2 induction cycles) included 49 patients (91%) with median age: 59.2 yrs; baseline Karnofsky performance status $\geqslant$80: 96%; stage T3/T4: 41%; lymph node positive: 43%; median time from surgery to inclusion was 43 days. Forty six patients (85%) received. the 6 planned induction cycles and 41 patients (76%) completed chemoradiation. The recurrence free 1-year survival rate is estimated at 71% (95% CI [0.581; 0 845]). Median dose intensity during induction: Gem 0.93, Ox 0.92, during chemoradiation: Gem 0.98. Forty one patients (98% of the irradiated population) received the total 50 Gy radiation dose.
The most frequent Gr 3/4 toxicities during induction chemotherapy (N = 51) were: hematological 29% (neutropenia 18%, thrombocytopenia 14%), nausea, vomiting, diarrhea:16%. Acute Gr 3/4 toxicities during chemoradiation (N = 42): neutropenia 19%, thrombocytopenia 7.0%. No toxic death occurred on treatment.
Conclusion: This adjuvant GemOx regimen combined with Gem-based chemoradiation was well tolerated during the two treatment phases with an encouraging 71% 1 year RFS. The late toxicities and OS will be analyzed after the end of the 2 years follow-up period. Mature results, will be presented during the meeting.