considered sufficient to give an 80% probability of rejecting a baseline clinical benefit rate of 55%, with an exact 5% one-sided significance test when the true disease control rate was 75%. The drug regimen would have been considered interest if at least 26 patients showed clinical benefit. Neoadjuvant induction chemotherapy (CHT) encompassed gemcitabine (GEM) 1000 mg/m^2 (100-min infusion on d1) and oxaliplatin 100 mg/m^2 (2-hr infusion on d2) every 2 wks, for 6 cycles. After CHT pts were restaged for surgery and/or chemoradiation (CRT) consolidation (EBRT up to a total dose of 50.4 Gy plus concomitant GEM 300 mg/m^2/week). After CRT completion, pts were restaged to evaluate secondary surgery.

Results: From January 2005 to January 2012, 35 pts (M/F: 17/18; median age: 68 yrs, range: 46-78; ECOG PS 0-1/2: 28/7) entered the study. A median of 5 (range 1-7) CHT induction cycles were delivered. Toxicity was mild, with G3-4 neutropenia in 2 pts (6%), G3 thrombocytopenia in 1 pt (3%), G3 transaminase elevation in 5 pts (14%), and G3 diarrhea in 2 pts (6%). CHT dose was reduced or delayed in 8 and 7 pts, respectively. Nine confirmed PR and 17 SD were observed for a CB of 74% (95% confidence interval [CI], 56.7-87.5%). A decrease in serum CA 19.9 ≥50% of the baseline was observed in 14 of 23 evaluable pts. Nine-teen pts completed CRT, including 5 pts who subsequently underwent surgery; 1 pt underwent surgery without CRT. Toxicity for the CRT phase was mild, with G3 thrombocytopenia in 1 pt (3%) and G3 neutropenia in 3 pts (8%). Median overall survival (OS) and progression free survival (PFS) for all 35 patients were 10 (95% CI, 8-12) and 9 mos (95% CI, 6-12), respectively. One-yr OS and PFS rates were 26% and 30%, respectively.

Conclusions: The regimen under study is active and well tolerated. Although an encouraging response rate was reported, OS remains poor, calling for a better selection strategy for LAPC pts who are candidates to neoadjuvant treatment.

Disclosure: All authors have declared no conflicts of interest.

714P MODIFIED FOLFOXIRI IN ADVANCED PANCREATIC CANCER

L. Ginocchi, E. Vasile, S. Caponi, M. Lucchesi, C. Caparello, V. Da Prat, M. Baretti, M. Lencioni, S. Ricci, A. Falcone

Oncologia, Trapianti e Nuove Tecnologie in Medicina, Polo Oncologico - Azienda Ospedaliero-Universitaria Pisana - Istituto Toscano Tumori, Pisa, ITALY

Background: The combination regimen of 5-fluorouracil/folinic acid, oxaliplatin and irinotecan named FOLFIRINOX has been proposed as a new standard of care for metastatic pancreatic cancer patients. However, FOLFIRINOX was associated with high incidence of grade 3 and 4 toxicities (neutropenia in 45.7% of patients with G-CSF use in 42.5% of patients; febrile neutropenia in 5.4%; diarrhea in 12.7%). Our group had developed a very similar schedule in colorectal cancer named FOLFOXIRI which contains no bolus 5-fluorouracil and a slight lower dose of irinotecan.

Methods: The objective of this study was to prospectively evaluate the tolerability and activity of a modified (m) FOLFOXIRI regimen in metastatic or locally advanced pancreatic cancer patients. The regimen included a lower dose of irinotecan (administered at 150 mg/sqm on day 1 every 14 days) and of infusional 5-fluorouracil (2800 mg/sqm administered as a 48-hour continuous infusion on days 1 to 3 every 14 days). Folinic acid and oxaliplatin remained unchanged.

Results: Thirty-nine patients with cytological or histological diagnosis of pancreatic adenocarcinoma have been treated with mFOLFOXIRI from august 2010 onwards; 17 had metastatic disease while 22 had locally advanced disease. A total of 260 cycles have been administered so far. The grade 3-4 toxicities reported are: neutropenia in 35.9% of patients; thrombocytopenia 2.6%; diarrhea 5.1%; stomatitis 7.7%; nausea/vomiting 5.1%; fatigue 2.6%; liver toxicity 5.1%; sensory neuropathy 5.1%. No toxic deaths and no febrile neutropenia have been occurred. G-CSF has been used in seven patients (18%). A delay in the administration of chemotherapy was required in 12 patients (31%) and a reduction of doses in 7 cases (18%). Among 30 evaluable patients 11 partial responses (36.7%) and 14 stable disease (46.7%) have been observed. Median progression-free survival (PFS) was 11.5 months and median overall survival (OS) 25.5 months. For metastatic patients only, response rate resulted 33% with a PFS and OS of 8.4 and 14.8 months, respectively.

Conclusions: The mFOLFOXIRI regimen as we used resulted feasible and quite well tolerated and it maintained its good activity in metastatic pancreatic cancer.

Disclosure: All authors have declared no conflicts of interest.

715P TIMING AND PATTERNS OF DISEASE PROGRESSION FOLLOWING CONCURRENT RADIOCHEMOTHERAPY IN PATIENTS WITH UNRESECTABLE LOCALLY-ADVANCED PANCREAS CANCER

C. Parlak[1], O.C. Guler[1], O. Ozyilkan[2], E. Topkan[1]

[1]Department of Radiation Oncology, Baskent University Adana Medical Faculty, Adana, TURKEY, [2]Medical Oncology, Baskent University Faculty of MedicineAdana Uygulama Ve Arastirma Mer., Adana, TURKEY

Background: Timing and patterns of disease progression in patients with unresectable locally-advanced pancreas carcinoma (LAPC) treated with definitive concurrent radiochemotherapy (C-RCT) was analyzed.

Materials and method: Fifty-two patients with histologic proof of LAPC underwent 50.4 Gy (1.8 Gy per fraction) of C-RCT with 5-FU followed by maintenance gemcitabine. Disease was considered to be unresectable if contrast-enhanced CT or staging laparoscopy/laparotomy revealed a low likelihood of complete resection and/or any of the following: involvement of superior mesenteric artery/cealiac trunk, encasement of 180 degrees or more of the circumference of superior mesenteric/portal vein, and/or evidence of narrowing of or thrombus within the superior mesenteric/portal vein. Elective nodal irradiation was not adopted. Primary aim was to assess timing and patterns of disease progression.

Results: Treatment was well tolerated and all patients were able to receive intended C-RCT regimen. At median 17.4 months of follow-up 38 (73.1%) were dead. Median, 1- and 2-year overall- and progression-free survival estimates were 16.1 months, 61.2% and 22.6%, and 7.4 months, 27% and 12.3% respectively. Analysis for timing of disease progression revealed that 7 (13.5%), 15 (28.8%), 20 (38.5%), and 22 (42.3%) patients experienced disease progression at 3, 4, 5, and 6 months, respectively, since initiation of R-RCT. Interestingly, although there were no isolated local or regional failures during this early follow-up period, all failures were presented as distant metastases with/without local/regional disease progression.

Conclusion: Results of this study demonstrated that, despite aggressive staging and treatment strategies, early distant disease progression are common source of treatment failures in unresectable LAPC. Present findings impact the urgent need for more efficacious chemotherapeutic agents for control of distant metastatic tumor deposits and better treatment strategies, such as induction chemotherapy followed by C-RCT, to eliminate early treatment failures and unnecessary and futile C-RCT in metastatic disease state.

Disclosure: All authors have declared no conflicts of interest.

716P FOLFIRINOX FOR LOCALLY ADVANCED PANCREATIC ADENOCARCINOMA. RESULTS OF AN AGEO MULTICENTRIC PROSPECTIVE STUDY

L. Marthey[1], A. Sa-Cunha[2], J.F. Blanc[3], A. Cueff[4], E. Francois[5], I. Trouilloud[6], D. Malka[7], J. Bachet[8], R. Coriat[9], J. Taieb[10]

[1]Gastroenterology, Bicêtre Hospital, Kremlin Bicêtre, FRANCE, [2]Digestive Surgery, Haut Lévêque Hospital, Pessac, FRANCE, [3]Digestive Oncology, Saint André Hospital, Bordeaux, FRANCE, [4]Biostatistics and Epidemiology, Georges Leclerc Cancer Institute, Dijon, FRANCE, [5]Medical Oncology, Antoine Lacassagne Cancer Institute, Nice, FRANCE, [6]Digestive Oncology, European Georges Pompidou Hospital, Paris, FRANCE, [7]Medical Oncology, Gustave Roussy Cancer Institute, Villejuif, FRANCE, [8]Gastroenterology, Pitié-Salpêtrière Hospital, Paris, FRANCE, [9]Digestive Oncology, Cochin Hospital, Paris, FRANCE, [10]Oncologie Digestive, Hopital Europeen Georges Pompidou, Paris, FRANCE

Background: The FOLFIRINOX regimen improves survival when compared to gemcitabine as first line treatment for patients (pts) with metastatic pancreatic cancer (1). There is no such data in non resecable, non metastatic, locally advanced pancreatic adenocarcinoma (LAPA). The aim of this study was to evaluate the safety and efficacy of FOLFIRINOX in this setting.

Methods: From February 2010 to February 2012, all pts from eleven French hospitals, who started FOLFIRINOX for a pathologically proven LAPA were included in a prospective database. Non resectability was determined by each local multidisciplinary staff. The absence of metastases was assessed by TAP CT-scans. FOLFIRINOX was administered every 2 weeks (oxaliplatin 85 mg/m^2; irinotecan 180 mg/m^2; leucovorin 400 mg/m^2; fluorouracil 400 mg/m^2 as bolus and 2400 mg/m^2 as 46-hour continuous infusion).

Results: Seventy seven pts were enrolled. We report the preliminary analysis of the first 53 pts as data collection is still ongoing. Patients characteristics were M/F: 30/23; median age 63 (46-79); PS 0/1/2 : 24/28/1. twenty one pts had a bilary stent before starting treatment. The median number of cycles administered was 5 (1-30). There were no treatment-related deaths and 8% of pts stopped treatment because of toxicity. Grade 3-4 toxicities were neutropenia (15%), nausea (13%), diarrhea (8%), anemia (2%), and thrombopenia (2%). Grade 2-3 sensitive neuropathy occured in 19% of pts. Dose reduction was necessary in 28% and prophylactic GCSF was used in 86% of pts. Partial response rate was 30% [95 CI% 17%-43%], and 53% of pts showed stable disease [95% CI 39%-67%], resulting in a disease control rate of 83% [95% CI 73%-93%]. Closure external radiotherapy was performed in 62% of pts and 32% underwent surgical resection of their tumour. With a median follow up of 8.5 months [95% CI 7-11], median overall and progression free survivals have not been reached. One year overall and progression free survival rates were 80% [95% CI 57%-92%] and 54% [95% CI 29%-74%], respectively.

Conclusion: FOLFIRINOX in LAPA seems efficient with a manageable toxicity profile and led to secondary potentially curative surgery in approximately one third of the pts. These promising results are encouraging to test this regimen in a phase 3 trial. (1) Conroy et al. NEJM 2011; 364: 1817

Disclosure: All authors have declared no conflicts of interest.