acute toxicity and patterns of failure in patients that receive chemoradiation (CRT) for inoperable cancer of the pancreas, after non-progression on C. Conformal RT is delivered, but elective nodal irradiation is omitted.
Material and Methods: All patients received neo-adjuvant C, if tolerated at least 6 months were delivered. CRT followed this if no evidence of progressive disease was found. A dose of 45−54 Gy in 1.8 Gy/fraction was delivered with 3D conformal planning. The planning target volume (PTV) was limited to visible tumour with 1.5 cm circumferential and 2 cm cranio-caudal margin. Elective nodes were not included. Toxicities were recorded prospectively during treatment. Local progression was defined as failure within PTV and local nodes, systemic as visceral disease present. Time to progression (TTP) and overall survival (OS) are reported from the date C was started.
Results: 45 patients, M/F = 23/22; median age 61 years (range 41−83) treated between 01/1997 and 12/2006. Stage IIb = 6, III = 39; ECOG PS 0−1/2/NA = 34/6/5; CA19.9 < 100 = 24, >100 = 21. C consisted of protracted infusion 5FU modulated with other agents (PVI5FU) = 14, Capecitabine (X) = 3, Gemcitabine (G) = 13, G+X = 15. A median of 6.6 months (range 1−16.8) of C were delivered. Median dose of RT 50.4 Gy, range (23.4−54). 27 patients received C with RT (19 X, 7 PVI5FU, 1 G). RT stopped due to toxicity in 2 patients (23.4 Gy, 46.8 Gy). 6 patients had breaks in RT: 2 non-compliance (4 days), 4 due to toxicity (2−28 days). During CRT 13 (28.8%) patients had grade 3 toxicities, 9 (20%) patients GI toxicity: (nausea = 6, vomiting = 2, diarrhoea = 1); fatigue = 2, abdominal pain due to tumour = 3, sepsis = 4, skin = 2, other = 3. One patient had grade 4 vomiting and 1 patient died shortly after RT due to perforated duodenal ulcer in RT field. 5 had C stopped or dose reduction during RT. The first site of failure was local in 8 patients, local and systemic in 6 and systemic in 22 patients. Median TTP was 13.5 mo; median survival 19.7 mo, 1-year OS = 79%, 2-yr OS = 28%.
Conclusion: Sequential C then CRT shows promising efficacy in the treatment of LAPC in a highly selected group of patients. The low proportion of local failures indicates that prophylactic nodal irradiation could be omitted to facilitate delivery of CRT.

3532 POSTER

Histopathological response to preoperative chemoradiation for resectable pancreatic adenocarcinoma: the French phase II FFCD 9704-SFRO trial

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Background: To define and evaluate histopathological response rates with preoperative chemoradiation (RT-CT) for resectable pancreatic adenocarcinoma.
Materials and Methods: Forty-one patients (pts) with localized, potentially resectable pancreatic adenocarcinoma were treated with 50 Gy combined with 5-Fluorouracil (300 mg/m^2 /d; d1-d5; week 1−5) and Cisplatin (20 mg/m^2/d; d1-d5 and d29-d33). Radiographic restaging was performed 4 to 6 weeks later and pts presenting with resectable disease underwent surgical resection.
Results: Twenty-six (63%) of 41 pts underwent curative surgery. Standardized histologic response was measured and graded by a single pathologist. The effectiveness of the preoperative chemoradiation was defined by the proportion of severly degenerative cancer cells (SDCC), their density and histological distribution and the proportion of necrotic tumoral tissue. Eleven of 24 (46%) specimens presented more than 80% of SDCC, and 8/11 (72%) specimens were associated with large necrosis areas. The histologic distribution was characterized by the low density of nonaffected cancer cells, and an important fibrous and amorphous connective tissue associated with cancer-cells' defects (type A of the Ishikawa's classification). Histologic complete response was observed in one specimen, and 9/24 (37%) specimens were characterized by 50 to 80% of SDCC. Finally, 4/24 specimens presented with a low rate of SDCC, few necrosis area and several non affected cancer cells (Ishikawa C).
Conclusion: Preoperative 5-Fluorouracil-Cisplatin-based concurrent RT-CT for resectable pancreatic adenocarcinoma provides antitumoral effect. With regard to the feasibility of this therapeutic schedule and the rate of major histologic response, this approach could offer a clinical benefit. Further gemcitabine-based chemoradiation regimens, will determine the predictive factors of the treatment response, and the improvement in survival. This study is the first in Europe to present histopathological data on a prospective approach.

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Cetuximab plus Gemcitabine/Oxaliplatin (GEMOXCET) in 1st line metastatic pancreatic cancer – a multicenter phase II study

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Background: Targeting the epidermal growth factor receptor (EGFR) pathway in pancreatic cancer seems to be an attractive therapeutic approach. The present study assessed for the first time the efficacy of cetuximab plus the combination of gemcitabine/oxaliplatin in metastatic pancreatic cancer.
Methods: Eligible subjects had histological or cytological diagnosis of metastatic pancreatic adenocarcinoma. The primary endpoint was response according to RECIST. Patients (pts) received cetuximab 400 mg/m^2 at first infusion followed by weekly 250 mg/m^2 combined with gemcitabine 1000 mg/m^2 as a 100-minute infusion on day 1 and oxaliplatin 100 mg/m^2 as a 2-hour infusion on day 2 every 2 weeks.
Results: Between January 2005 and August 2006 a total of 64 pts [22 women (34%), 42 men (66%); median age 64 years (range 31−78)] were enrolled at 7 study centers. At April 2007 a total of 37 pts are still alive. 58 pts are evaluable for baseline and toxicity analysis. 6 pts had no treatment or an incomplete drug combination within the first cycle of the treatment plan (n = 3 hypersensitivity reactions to the first cetuximab infusion, n = 1 rapid tumor progression, n = 2 lost of follow-up). Reported grade 3/4 toxicities (% pts) were: leucopenia 12%, anemia 16%, thrombocytopenia 11%, diarrhea 7%, nausea 14%, infection 19%, allergy 4%. Cetuximab-attributable skin reactions occurred as follows: grade 0: 28%, grade 1: 43%, grade 2: 22%, grade 3: 7%. The intention-to-treat analysis of 50 evaluable pts shows an overall response rate of 32% including 1 (2%) complete and 15 (30%) partial remissions. There were 30% pts with stable and 38% pts with progressive diseases or interruption of the therapy. Median time to progression is 123 days with a preliminary overall survival estimation of 8 month. A clinical benefit response was noted in 23 of evaluable 54 pts (43%).
Conclusion: The addition of cetuximab to the combination of gemcitabine and oxaliplatin is well tolerated and exhibits a high response rate. Further evaluation in a phase III trial is warranted.

3534 POSTER

Patients with ERCC1-negative tumors may benefit from preoperative CRT in resectable esophageal cancer

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Background: We reported that preoperative chemoradiotherapy (CRT) did not show survival advantage to surgery alone in general patients with resectable esophageal cancer (Lee JL et al., Ann Oncol 2004;15:947−54). We investigated the effects of preoperative CRT on survival according to ERCC1 status in resectable esophageal cancer.
Materials and Methods: Paraffin-embedded pretreatment tumor specimens, collected by endoscopic biopsy from patients treated either with surgery alone or with preoperative CRT (5-FU/cisplatin or capecitabine/cisplatin with 46.5−48 Gy of radiation) followed by surgery, were analyzed by immunohistochemical assay for ERCC1. Staining intensity and proportion of ERCC1 were graded on a scale of 0 to 3, and the resulting scores were multiplied to obtain a semiquantitative score (0−9).
Results: Between March 1993 and June 2005, 175 patients were treated with preoperative CRT followed by surgery or surgery alone as part of prospective clinical trials. Of those, 152 biopsy specimens (111 in the