of the irradiated volume 12 months after treatment. Nine patients had new hepatic tumors, solitary in 1 patient and multiple in 8, exclusively outside the irradiated volume 4–29 months after proton beam therapy. Subsequently, 2 of the 10 patients with new hepatic tumors received second proton beam therapy and the irradiated new tumors were controlled. Consequently, all patients but one died 3–63 months after proton beam therapy; the causes of death were cancer in 6 patients, liver failure in 8, intracranial hemorrhage in 2, and interstitial pneumonitis and trauma in 1 each. The remaining 1 patient was alive with no evidence of disease 33 months after proton beam therapy. The overall and progression-free survival rates were 53% and 47% at 1 year, respectively, and 42% each at 2 years. Performance status and Child-Pugh score were significant prognostic factors for survival. Therapy-related toxicity of grade 3 or more was not observed.
Conclusions: Proton beam therapy for HCC patients with severe cirrhosis was effective and tolerable. It appeared to have achieved good local control and improved survival for the patients.

789 PUBLICATION

The FOLFIRI.3 regimen (5-FU/ folinic acid plus CPT-11) in advanced pancreatic carcinoma (PC): results of an AGEO* phase II study

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Background: New therapies are clearly needed to improve the prognosis of patients (pts) with advanced PC. The rationale to develop the FOLFIRI.3 regimen is based on pre-clinical experiments on cell cultures and human tumor xenografts indicating optimal synergy between CPT-11 and fluorouracil when CPT-11 is given before and after 5-FU.
Methods: 35 pts with non pre-treated locally advanced (LA) or metastatic (M) PC were prospectively enrolled. They received a FOLFIRI.3 regimen: CPT-11 90 mg/m* d1 and d3, folinic acid 400 mg/m* on a 2h00 infusion and continuous 5-FU 2000 mg/m* from d1 to d3. Treatment was repeated every two weeks until disease progression or limiting toxicity. Eligibility criteria were: pathologically proven PC, PS (ECOG) 0–2, age $\geqslant$18, measurable disease, serum bilirubin <1.5 UNL, adequate hematological and renal functions.
Results: 31 pts are currently evaluable for toxicity and 29 for efficacy. Patient's characteristics were M:18 pts/F:13 pts; LA:7 pts/ M:24 pts; mean age: 58 years (42–77) and initial performance status (WHO) was 0/1/2 in 8/14/9 pts, respectively. No Toxic death occurred. Hematological grade 3–4 toxicities consisted in neutropenia (32%), including two febrile neutropenia. Only 1 grade 3 thrombocytopenia (3%) and anemia (3%) were seen. Grade 3–4 non hematological toxicities were nausea vomiting (35%) and diarrhea (29%). Grade 2 alopecia was observed in 14 pts (45%). Eleven objective responses (35%) were observed, one leading to a surgical resection of the tumor. CA 19.9 decreased (>50%) in 56% of the patients with initially elevated CA 19.9. Nine (29%) stable disease and 9 PD (29%) were observed and 2 pts were not evaluable. With a mean follow-up of 9 months, median progression free and overall survival were 6.7 (CI:5–12.1) and 13.8 months (CI: 5.5–17.9), respectively.
Conclusion: With a 35% overall response rate and manageable toxicity the FOLFIRI.3 regimen seems to be an active regimen in non pre-treated advanced PC pts.

790 PUBLICATION

Neoadjuvant chemotherapy can eradicate lymph node micrometastasis for squamous cell carcinomas of the thoracic esophagus

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Background Data: Neoadjuvant chemotherapy has been postulated but not yet proved to eradicate micrometastasis and improve prognosis of patients with advanced squamous cell carcinomas of the thoracic esophagus (ESCC).
Cytokeratin immunohistochemistry of the lymph nodes of ESCC revealed not only Micrometastases (MM) but also Cytokeratin Deposits (CD), which are hyalinized and de-nucleated particles, considered to be the cadaver of carcinoma cells. Successful chemotherapy should convert cancer cells from MM to CD and ESCC patients from systemic disease to regional disease.
Methods: Cytokeratin immunostaining of surgically removed lymph nodes were performed for 100 patients with node-positive ESCC patients, including 25 patients treated with surgery alone (Surgery Group) and 75 patients undergone neoadjuvant chemotherapy using CDDP, Adriamycin and 5Fu (NACT group). Cytokeratin positive staining was referred to serial hematoxylin-eosin stained sections and classified as metastasis, MM and CD.
Results: CD was less frequently observed in Surgery group than in NACT group (8% vs 47%, $p = 0.0024$), while MM tend to be higher in the former (52% vs 40%). MM was a poor prognostic factor in both Surgery and NACT group, while CD was a favorable prognostic factor in NACT group. Effect of NACT on MM were considered to be eradicated: MM(−)/CD(+), persistent: MM(+)/CD(+), no effect: MM(+)/CD(−) and not informative: MM(−)/CD(−). This classification was well correlated with clinical response of main tumor, number of lymph node metastasis in the surgical specimen and post operative survival (3 year survival: 78%, 18%, 0% and 38% respectively). MM(−)/CD(+) was a significant prognostic factor as well as number of lymph node metastasis in the multivariate analysis.
Conclusion: Disappearance of MM and emergence of CD might suggest the eradication of MM by NACT. Clinical benefit of NACT was apparent for these patients with node positive ESCC.

791 PUBLICATION

A phase II study of gemcitabine and oxaliplatin in combination with celecoxib in patients with advanced pancreatic tumors overexpressing cyclooxygenase-2 (COX-2)

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Introduction: Overexpression of the COX-2 enzyme has been reported in 90% of patients with advanced pancreatic cancer.
COX-2 contribute to tumor growth through angiogenesis and may be implicated in gemcitabine and oxaliplatin resistance by increasing expresion of NK-kB.
Gemcitabine and oxaliplatin (GEMOX) is an active regimen in pancreatic cancer.
The aim of this study is to evaluate the activity and toxicity of GEMOX plus celecoxib in advanced pancreatic cancer.
Patients and methods: A phase II study according to Fleming regimen was used: 43 patients should be included to demonstrate an increase in response rate of 10% in comparison with the response obtained by GEMOX regimen (for an overall response rate of 40%).
Patients with metastatic and/or advanced disease were eligible for the study. All patients should have COX-2 by immunohistochemistry or cytochemistry.
Tumor response was assessed by RECIST criteria with CT imaging every 3 cycles. Ca 19–9, pain assessment and QoL assessment were performed every cycle.
The patients received gemcitabine 1000 mg/mq on day 1 and oxaliplatin 100 mg/mq on day 2 every 14 days. Celecoxib was administered at the dose of 400 mg/mq bid through the entire cycles.
Results: Forty-three patients (median age 57 years) were enrolled of which 15 local and 28 metastatic.
The most common grade 3/4 toxicities included: diarrhea 3/43, nausea and vomiting 4/43, neutropenia 5/43, and 3/43 peripheral neuropathy. A marked decrease in elevated baseline CA19.9 (>50%) was observed in 12 patients (27.9%). 13/43 (30.2%) patients reported an improvement in quality of life. Six patients achieved a partial response (13.9%) and 28 (65.1%) showed a stable disease. The overall median time to progression was 4 months and median survival was 9.5 months.
Conclusion: In conclusion, the addition of celecoxib does not seem to increase the activity even in tumors overexpressing COX-2.

792 PUBLICATION

Preliminary results of a phase II trial of dose-intense PEFG (cisplatin, epirubicin, 5-fluorouracil, gemcitabine) in advanced pancreatic adenocarcinoma

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Background: PEFG regimen was superior to standard gemcitabine in a phase III trial (Reni M Lancet Oncol 2005) in advanced pancreatic adenocarcinoma (PA). This regimen was subsequently modified by increasing dose-intensity (Dell'Oro S, Ann Oncol 2004). The aim of the present study was to assess activity and feasibility of dose-intense PEFG regimen.