

(TIL p: 0.0087) none of the other examined factors affected local recurrence rate in the present series: nodal status (NS p: 0.83), lateral spreading (LS p: 0.76), lymphatic vessel invasion (LVI p: 0.347), blood vessel invasion (BVI p: 0.197), perineural invasion (PI p: 0.22). On the other hand overall survival is correlated with most of the above mentioned parameters and is inversely matched with the presence of lymphocyte infiltrate (TIL p: 0.0001, NS p: 0.0028, LS p: 0.0067, LVI p: 0.058, BVI p: 0.352, PI p: 0.0003).

**Conclusions:** The present data are indicating the lymphocyte infiltration as a major prognostic factor in predicting the risk of local or distant relapse in rectal cancer patients.

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PUBLICATION

# **Oncological results of hepatectomy associated with radiofrequency ablation of strictly unresectable liver metastases T in 63 patients with colorectal primary**

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**Background:** Results and indications of intra-operative radiofrequency (RF) ablation of liver metastases (LM) are not well defined in the literature. **Aim:** To appreciate the survival rate of patients with strictly unresectable LM (defined on technical but not oncological criteria) when undergoing liver resection plus RF, along with recent systemic chemotherapy.

**Patients and methods:** Sixty three patients with technically unresectable LM (either >5, or bilateral with no sparing at least one sector of the liver, or with tumor proximity to central major vascular structures) were treated by segmental anatomic resection (44 patients, 142 LM) when LM were large, with wedge resection (36 patients, 55 LM) when LM were peripheral and small, and with RF (63 patients, 154 LM) when LM were central and small. Extrahepatic metastases were also resected in 27%. All patients received perioperative chemotherapy. The median follow-up was 27.6 months (range: 15–74).

**Results:** There was no postoperative mortality and the morbidity rate was 27%. The 2-year overall survival rate of the 63 patients was 67% with a median survival of 36 months. In comparison, the median survival of similar patients treated classically with systemic chemotherapy alone is (was?) 18 months. The local recurrence rates were similar for the 3 types of local treatments: 7.1% for the 154 RF ablations, 7.2% for the 55 wedge resections, and 9% for the 44 segmental anatomic resections (p = 0.216). Hepatic recurrences occurred in 71% of patients.

**Conclusion:** The combination of anatomic segmental resection, wedge resection, RF ablation, and recent systemic chemotherapy in patients with really unresectable LM results in a median survival of 36 months, and appears as a real improvement in survival.

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# **Chemoradiation with raltitrexed in preoperative treatment of stage II/III resectable rectal cancer: long term results of a phase II study**

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**Background:** Aim of this study is to evaluate the impact of a neoadjuvant chemoradiation with raltitrexed on tumor response and long term results, in patients with locally advanced resectable rectal carcinoma.

**Material and methods:** Between 1998 and 2002, 39 patients were treated with preoperative chemoradiation, IV bolus of raltitrexed on days 1, 19 and 38 and concurrent 50.4 Gy (1.8 Gy/day) external beam radiotherapy. Surgery was performed 6–8 weeks after the end of chemoradiation. A 10 Gy IORT boost was delivered to the tumor bed. Patients with positive nodes at pathological examination underwent adjuvant with 5-FU-leucovorin (Machover regimen).

**Results:** All patients had T3 tumor at diagnosis, the N stage was: cN0 9 patients, cN1 19 patients and cN2 11 patients. All patients underwent surgery. The median follow-up was 58 months (range 34–79). Of 39 patients 24 (61%) downstaged at T level and 27 (69%) at N level. The pT stage was pT0 9 patients (23%), pTmic 7 patients (18%), pT1 2 patients (5%), pT2 6 patients (16%), pT3 13 patients (33%), and pT4 2 patients (5%). According to TRG (Tumor Regression Grade) classification patients were: TRG1 23% (9/39), TRG2 18% (7/39), TRG3 38% (15/39), and TRG4 21% (8/39). Five years OS was 91.7%, LC was 97.4% and MFS was 72.2%. Patients were grouped according pT (T0–2 vs T3–4), TRG (TRG1–2 vs TRG3–4), cN (cN1–2 vs cN2) and pN stage (pN0 and pN+). The cN stage wasn't statistically correlated with 5-year outcomes: OS was equal in the two group of patients; LC was 100% and 90.0% in cN0–1 and cN2, respectively; MFS was 78.5% in cN0–1 and 54.5% in cN2. Of postoperative parameters pT didn't show correlation with OS, a difference, even if not significant, was found for LC (100% in pT0–2 vs 93% in pT3–4) and MFS

(82% in pT0–2 vs 58.7% in pT3–4); TRG showed a not statistical correlation with LC (100% in TRG1–2 vs 95.5% in TRG 3–4) and MFS (93.7% in TRG1–2 vs 61% in TRG 3–4), OS was equal in the 2 group of patients; pN was the strongest post-treatment factor in influencing the outcomes at 5 years: OS was 91.7% and 77% in pN0 and pN+ patients respectively (p = ns), LC was 97.4% and 90% in pN0 and pN+ patients respectively (p = ns), MFS was 72.2% and 52.6% in pN0 and pN+ patients respectively (p = 0.025).

**Conclusion:** Preoperative chemoradiation with raltitrexed showed and high rate of tumor downstaging, with an elevated percentage of pathological major response (pT0-mic 41%). Results were excellent in terms of OS and LC. The 5-years MFS was 72.2% and was statistically correlated pN status. A longer follow-up is needed to confirm data. Validation of pretreatment prognostic factors will help to select patients to treat with more aggressive chemoradiotherapy combination.

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

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**Purpose:** 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.

**Patients and methods:** Thirty 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<sup>2</sup> 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<sup>2</sup> 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 patients have been included, mean age 57 years old (41–73), 20 male and 10 female, 30 are evaluable for toxicity. Concurrent radiation and twice-weekly gemcitabine at 30-, 40-, 50-, 60-, 70 mg/m<sup>2</sup> 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. This study currently explores the level 80 mg/m<sup>2</sup> twice a week.

**Conclusions:** This work is still in progress, until the MTD is reached. The complete cohort of patients will be finally analyzed for toxicity and for survival and relapse patterns, and will be followed by a phase II study to ascertain the feasibility of this scheme, with the recommended dose of twice-weekly gemcitabine, when evaluated. The next phase I trial will include oxaliplatin in addition to gemcitabine and radiation, for the same type of patients. Complete results will be presented during the meeting.

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# **Laminin-5-gamma2-chain during the colorectal adenoma-carcinoma sequence: from primary anchoring protein to an invasion promotor**

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**Background:** The glycoprotein Laminin-5 is a key protein of the epithelial cell adhesion complex, providing cell anchoring to the basement membrane in normal colorectal mucosa. The  $\gamma$ 2 chain of Laminin-5 (Ln-5  $\gamma$ 2) plays a pivotal role in cell migration and, possibly, as an invasion promotor in colorectal carcinomas. This study was performed to test whether there are and if yes, which changes occur in immunohistochemically detected Ln-5  $\gamma$ 2 pattern during the malignant transformation of colorectal adenomas.

**Material and Methods:** Paraffin specimens of full rectal wall specimens of low (n = 55) and high grade (n = 13) neoplastic colorectal adenomas, colorectal carcinomas (n = 37) and normal colon (n = 60) were assessed histopathologically and immunohistochemically for Ln-5  $\gamma$ 2 changes using the monoclonal antibody D4B5.

**Results:** A significant increase of immunohistochemically detected Ln-5  $\gamma$ 2-alterations associated with migration and invasion were described, i.e. loss of Ln-5  $\gamma$ 2 to the basement membrane, stromal deposition and intracellular increase of Ln-5  $\gamma$ 2 from low grade neoplastic adenoma to