

for local control ( $p < 0.0003$ ) followed by radiation technique (conformal >conventional) ( $p < 0.02$ ). Tumor distribution and acute treatment toxicities data from the two techniques are shown in Table 1.

**Conclusion:** Conformal therapy contributes significantly in the local control and improves the therapeutic index of patients with anal canal cancer. It is now the standard technique at our institution.

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POSTER

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

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**Purpose:** To define and evaluate histopathological response rates with preoperative chemoradiation (RT-CT) for resectable pancreatic adenocarcinoma.

**Patients:** Between January 1998 and March 2003, 41 patients (pts) (25 males; mean age: 59 years; range: 33–75) with localized, potentially resectable pancreatic adenocarcinoma were treated with 50 Gy combined with 5-Fluorouracil (300 mg/m<sup>2</sup>/d; d1-d5; week 1–5) and Cisplatin (20 mg/m<sup>2</sup>/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. According to the difficulty to characterize viable cells by conventional anatomopathological evaluation, the effectiveness of the preoperative chemoradiation was defined by the proportion of severely degenerative cancer cells (SDCC), their density and histological distribution and the proportion of necrotic tumoral tissue. SDCC cancer cells were defined by a nuclei absent, piknotic or irregular-shaped, and an acidophilic or vacuolated cytoplasm. 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, principally located in the center of the tumor, 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, with fairly the same histologic distribution. Finally, 4/24 specimens presented with a low rate of SDCC, few necrosis area and several non affected cancer cells (type C of the Ishikawa's classification).

**Conclusion:** Preoperative 5-Fluorouracil-Cisplatin-based concurrent RT-CT for resectable pancreatic adenocarcinoma provides antitumoral effect, with 20/24 (83%) specimens presenting an histological response rate superior to 50% and one complete histopathologic response. 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.

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#### Randomized comparison of capecitabine plus oxaliplatin (CapOx) versus capecitabine plus gemcitabine (CapGem) versus gemcitabine plus oxaliplatin (GemOx) in advanced pancreatic cancer

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**Background:** Gemcitabine, oxaliplatin, and capecitabine are active agents in pancreas cancer. This study was performed to define an optimal regimen for combination therapy.

**Methods:** Between July 2002 and May 2004, 190 patients were recruited from 44 centres. Patients received 3-week regimens of either capecitabine 2 × 1000 mg/m<sup>2</sup> po d1–14 plus oxaliplatin 130 mg/m<sup>2</sup> iv d1 (CapOx) or capecitabine 2 × 825 mg/m<sup>2</sup> po d1–14 plus gemcitabine 1000 mg/m<sup>2</sup>

applied as a 30-min infusion d1+8 (CapGem) or gemcitabine 1000 mg/m<sup>2</sup> applied as a 30-min infusion d1+8 plus oxaliplatin 130 mg/m<sup>2</sup> d8 (GemOx). The primary endpoint of the trial was progression-free survival at 3 months. **Results:** Patients in the CapOx, CapGem, and GemOx-arms were well balanced according to the strata Karnofsky Performance status (KPS >70% in 92% vs 89% vs 90%) and stage of disease (metastatic disease in 76% vs 74% vs 75%). Median age was 63 years (range 37–75). Patients received a median of 4 cycles of treatment. In a per patient analysis of CapOx vs CapGem vs GemOx, hematological grade 3–4 toxicity occurred in 8%, 18%, and 21%, while non-hematological grade 3–4 toxicity was documented in 55%, 39%, and 51%, respectively. 167 patients were evaluable for response. The analysis of CapOx vs CapGem vs GemOx did not show any complete remission, while partial responses were obtained in 19%, 21%, and 12% of patients, and stable disease was documented in 33%, 41%, and 40% for a disease control rate of 52%, 62%, and 52%, respectively. Median PFS was comparable between CapOx, CapGem and GemOx treatment arms and amounted to 129 days, 143 days, and 102 days respectively with a median progression-free survival at 3 months of 54%, 59%, and 56%. Median overall survival for CapOx was 245 days, for CapGem 238 days, and for GemOx 206 days, respectively (two-sided logrank test,  $p = 0.57$ ).

**Conclusions:** The current evaluation of this trial indicates a comparable efficacy with regard to the primary endpoint and tolerability for the investigated regimens CapOx, CapGem, and GemOx.

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POSTER

#### Outcome of node negative gastric cancer personal experience on 278 patients

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In recent decades, the incidence of gastric cancer has declined, but the prognosis in the Western countries has not improved, the 5-year survival being 20–30%. Lymph node involvement is an important prognostic variable in gastric cancer. A surgical approach of potentially curable gastric cancer, including extended lymphadenectomy, seems to give better results when compared with less radical procedures. The therapeutic value of an extended lymphadenectomy is unproven in randomized trials; however, the high long-term survival rates reported by experienced centers after systematic, standardized extensive D2 and D3 gastrectomies are encouraging. In order to evaluate the outcome of node-negative gastric cancer who underwent curative gastric resection at San Raffaele Hospital of Milan, between 1987 and 2004.

**Materials and methods:** Patients: Between 1987 and 2004, 278 patients (157 males, 121, females) underwent a R0 gastric resection for gastric cancer, performed at the Department of Surgery, Vita-Salute San Raffaele University, Milan. The surgical procedure consisted of 39 (14%) total and 239 (86%) subtotal gastrectomies. A standard dissection encompassing N1 lymph nodes was defined as a D1 dissection, whereas complete removal of N2 lymph nodes was considered a D2 dissection. The extent of lymph node dissection was limited D1 ( $n = 120$ , 43%) or extended D2 ( $n = 152$ , 55%) and D3 ( $n = 6$ , 2%). The mean number of examines lymph nodes was 16.

Statistical analysis was carried out using the Statistical Package for the Social Sciences (SPSS 11.0). The results were expressed as mean ± SD. Overall survival was calculated according to the Kaplan-Meier method. Frequencies were compared by the Pearson's chi square method, and the multivariate analysis was performed using the Cox proportional hazards model, all with two sides at a significance level of  $p < 0.05$ .

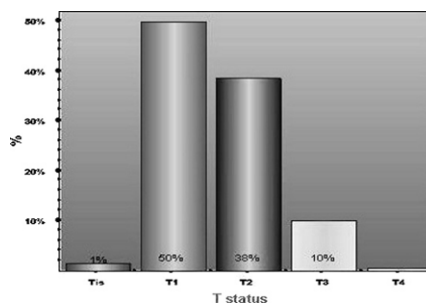


Fig. 1.

**Results:** The tumor stage was: T1 ( $n = 143$ ), T2 ( $n = 105$ ), T3 ( $n = 10$ ), T4 ( $n = 2$ ) (Fig 1). The median age of patients with node-negative gastric cancer was 65+/-11 years. The median tumour size was 3.8 cm (range

02, to 12). For the entire cohort the median number of lymph nodes per specimen was 16+/-11. The mean follow-up time was 60 months. The length of hospital stay was 14 days (range 5 to 100) with an in-hospital mortality rate of 1.3%. The overall-five years survival was 80% (74% and 82% in patients submitted to D1 and D2 lymphadenectomy, respectively;  $p = \text{ns}$ . Fig.2 (a-b).

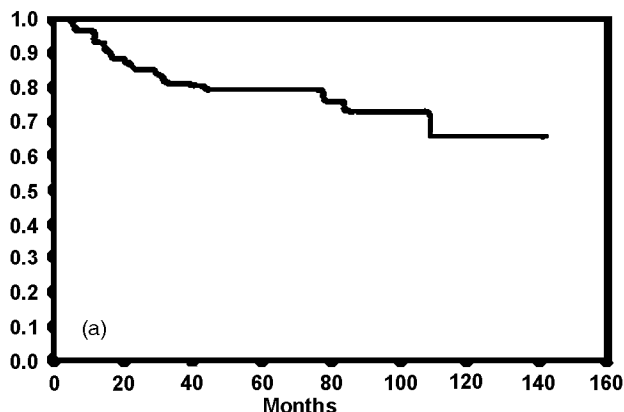


Fig. 2a.

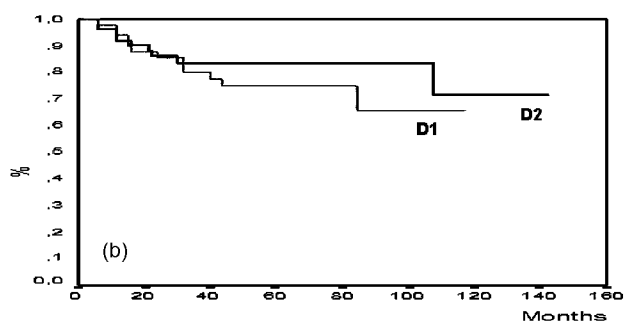


Fig. 2b.

In order to comparing survival, the follow factors were analysed for prognosis: extent of lymphadenectomy (D1 vs D2), patient age, tumor stage, tumor size. In the multivariate analysis only the tumor stage was predictor of outcome (Fig3).

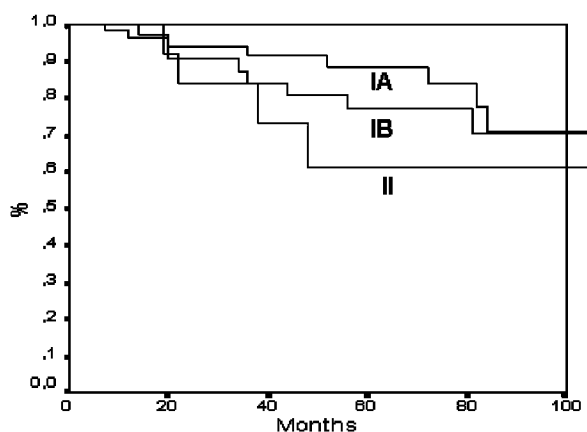


Fig. 3.

**Conclusions:** The high long-term survival rates reported by experienced centers after systematic, standardized extensive D2 and D3 gastrectomies are encouraging. In our center, D2 gastrectomy is become routine. However, in the multivariate analysis the extent of lymphadenectomy does not influence survival of patients submitted to gastric resection for node negative gastric cancer. In these patients, only T stage is closely related to the clinical outcome.

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### Chemotherapy in advanced gastric cancer: a systematic review and meta-analysis

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**Background:** Systemic chemotherapy is the major treatment option for the majority of gastric cancer patients. Uncertainty remains regarding the choice of the regimen.

**Materials and methods:** Our objectives were to assess the effect of

1. Chemotherapy versus best supportive care (BSC)
2. Combination versus single agent chemotherapy
3. The following different combination chemotherapy regimens:
  - a. 5-FU/cisplatin combinations with versus without anthracyclines
  - b. 5-FU/anthracycline combinations with versus without anthracyclines

on overall survival and toxicity.

**Search strategy:** We searched: Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, proceedings from DDW, ECCO, ESMO, ASCO until February 2005.

**Selection criteria:** Randomised controlled trials on systemic intravenous chemotherapy versus BSC, combination versus single agent chemotherapy and different combination chemotherapies as above in advanced gastric cancer.

**Results:** 24 randomised trials with a total number of 3304 patients are included in this meta-analysis. Analysis of 1. Chemotherapy versus BSC consistently demonstrated a significant benefit in terms of overall survival in favour of the group receiving chemotherapy (HR 0.39, 95%CI 0.28–0.52). Analysis of 2. Combination versus single-agent chemotherapy provides evidence for a survival benefit in favour of combination chemotherapy (HR 0.83, 95%CI 0.74–0.93), which is achieved at the price of increased toxicity. When comparing 3a.) 5-FU/cisplatin-containing combination therapy regimens with anthracyclines versus those without anthracyclines (comparison 4 including 501 patients: HR 0.77, 95%CI 0.62–0.95) and 3b.) 5-FU/anthracycline-containing combinations with cisplatin versus those without cisplatin (HR 0.83, 95%CI 0.76–0.91), both demonstrate a significant survival benefit for regimens including 5-FU, anthracyclines and cisplatin. Among these three-drug-regimens, the rate of treatment related deaths was higher when 5-FU was administered as bolus compared to infusional 5-FU (3.3 versus 0.6%).

**Conclusions:** Chemotherapy significantly improves survival in comparison to best supportive care. In addition, combination chemotherapy improves survival compared to single-agent 5-FU, but the effect size is much smaller. Among the combination chemotherapy regimens studied, best survival results are achieved with three-drug regimens containing 5-FU, anthracyclines and cisplatin. Among these, ECF (epirubicin, cisplatin, 5-FU) is tolerated best.

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## POSTER

### Lymph node ratio as prognostic factor in digestive tumours

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**Background:** The current TNM classification in digestive cancers uses different rules for the pathologic staging of regional lymph node involvement. For stomach, staging is based on the number of involved nodes, with N1 defined as 1 to 6 regional nodes involved, N2 as 7 to 15, N3 as 16 or more involved. For colon and rectum, N1 means 1 to 3 involved nodes, and N2, four or more. For anal canal, the staging is based on the anatomical location of the involved lymph nodes. For esophagus and other sites, N1 indicates involvement without any subdivision. The different rules can be confusing. It might be asked if a more unified approach can be considered. There is a growing literature suggesting that the lymph node ratio (LNR), defined as the proportion of nodes found involved among excised nodes, might give more accurate prognostic information. The present study investigates whether or not the LNR can be used to consistently define prognostic subgroups.

**Material and methods:** Data was abstracted from the Surveillance, Epidemiology, and End Results public use database 2004. Selection was histology confirmed primary invasive carcinoma diagnosed between 1988 and 1997, surgically resected. Retroperitoneum, peritoneum and unspecified organs were excluded. Three groups were defined based on