Proffered Papers

Gastro-intestinal

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Results of a randomised trial comparing ECF with MCF in advanced oesophago-gastric cancer

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Aims: To compare ECF with a new combination MCF for tumour response, survival, toxicity and quality of life (QL) in patients with previously untreated advanced oesophago-gastric cancer.

Methods: 580 patients were treated with ECF [epirubicin (50 mg/m^2) and cisplatin (60 mg/m^2) every 3 weeks with protracted venous infusion (PVI) 5-FU (200 mg/m^2/day for 24 weeks)] or MCF [mitomycin C C (7 mg/m^{2}6-weekly), cisplatin (50 mg/m^2 3-weeldy) and PVI 5-FU (300 mg/m^2/day for 24 weeks)].

Results: Overall response rate was 41% with both ECF MCF (p = 0.97). Response rates were higher for cancers of the OGJ (48%) than stomach (35%; p = 0.03). Toxicity was tolerable with only 2 toxic deaths. ECF caused more grade 3/4 neutropenia (p = 0.003); grade 3/4 thrombocytopenia was more common with MCF (p = 0.007). Alopecia was more common with ECF (p < 0.0001) whilst plantar-palmar erythema was more frequent with MCF (p = 0.017). Median failure free survival was 7 months with both ECF and MCF. Median survival was 9.4 months with ECF and 8.7 months with MCF (p = 0.89) and 1-year survival was 37% and 33% respectively. For patients with locally advanced disease median survival was 11.3 months with ECF and 11.5 months with MCF (p = 0.203) and 1-year survival was 41% and 48%. QL was superior with ECF compared to MCF after 12 and 24 weeks treatment

Conclusion: ECF and MCF result in equivalent response and survival but QL is superior with ECF. ECF remains one of the reference treatments for advanced oesophago-gastric cancer.

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Efficacy of 5FU + cisplatin (FUP) compared to bolus 5FU (FU) in advanced pancreatic carcinoma (APC)

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Chemotherapy (CT) with 5FU has a marginal efficacy in APC. However, FUP gave us a 27% response rate (RR) and 29% one-year survival (S) in a previous phase II study. We try to confirm the superiority of FUP over FU in this randomized study of the digestive group from the French Anticancer Centers (FNCLCC).

Population: APC histologically proven, measurable or evaluable, metastatic or locally advanced, non pretreated. Chemotherapy regimens were: – arm FU = 5FU: 500 mg/m"/day (d) × 5d every 4 weeks; – arm FUP: continuous infusion of 5FU 1000 mg/md": d × 5d + cisplatin: 100 mg/m" on d1 every 4 weeks

Results: 207 patients (pts) have been randomized by 18 centers, 103 in arm FU and 104 in arm FUP; there was no imbalance between arm FU and arm FUP. Median number of cycles: 2 vs 2 (range 0 to 14). Grade 3–4 toxicity (WHO) was lower in arm FU vs arm FUP: 20% vs 47% (p < 0.001); neutropenia: 6% vs 22%; vomiting: 4% vs 16%; mucositis: 5% vs 13%; toxic deaths: 1 vs 4 early in the trial. Efficacy: 6-month S for arm FU vs arm FUP were 28% vs 38%; one-year S: 8% vs 17% (logrank, p = 0.08), 6-month progression free S (PFS): 5% vs 19% (p = 0.0002). RR (intent to treat analysis) were 0% vs 12% (p < 0.01) (partial response: 0/97 vs 12/94 evaluable patients).

Conclusion: In APC with poor prognostic factors FUP is superior to FU in terms of RR and PFS. The low RR is partly related to the number of patients who received only one cycle. Even if non optimal this FUP regimen give interesting results, better tolerated regimens combining 5FU and P are needed.

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Locally advanced pancreatic carcinoma: Neoadjuvant radiochemotherapy (RCT) with 5-fu and mitomycin c

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Purpose: Rates of curative resection in locally advanced pancreatic carcinoma are low. We investigated if simultaneous RCT can be performed concerning acute toxicity and if operability can be produced.

Methods: 27 patients (pts) have been recruited for RCT between July 1995 and February 1998. Pancreatic carcinoma either was histologically proven or clinically suggested (CT, ERCP, CA 19-9). After exclusion of distant metastases 3d-conformal radiotherapy has been administered with 1.8 Gy daily. Primary tumour, metastatic nodes and high risk nodes were irradiated with a total dose of 50.4 Gy followed by a boost to 55.8 Gy. Simultaneously, we administered 2 courses of 5-FU (1000 mg/m^2 IV as 120 h continuous infusion, d1-5 and 29–33) and Mitomycin C (10 mg/m^2, IV bolus injection, d2 and d 30). Acute toxicity for radiotherapy (RTOG) and chemotherapy (NCI) have been registered. We report upon resectability and survival.

Results: RCT could be fully administered in 25/27 pts. In 2/27 pts it had to be aborted due to distant metastases occurring during treatment. Acute toxicity: upper GI tract 5/27 °III, 0/27 °IV; diarrhea 0/27 °III/IV; leukopenia 6/27 °III/ 1/27 °IV; thrombopenia 1/27 °III, 1/27 °IV; hemoglobine 2/27 stage III, 0/27 stage IV. R0-resection could be performed in 9/25 pts. Median follow-up is 20 mts. 6/25 pts are alive, 3/9 after resection and 3/16 without resection.

Conclusion: Neoadjuvant RCT is a promising therapeutic concept with low toxicity. 36% (9/24) with irresectable/borderline resectable tumours at diagnosis can be completely resected (R0).

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High incidence of K-Ras mutations in the bile fluids of patients with primary sclerosing cholangitis

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Primary sclerosing cholangitis (PSC) is associated in 10%–36% with cholangiocellular carcinoma (CCC). So far no reliable factors have been described which can define high risk PSC-patients for the development of CCC. Since K-Ras mutations occur early during the development of many cancers, we investigated the bile of PSC patients for K-Ras mutations as an possible prognosis factor.

Methods: 50 patients with PSC and 19 patients with other benign cholestatic liver diseases (benign choledochusstenosis after OLT (1I), liver cirrhosis (3), choledocholothiasis (4), Budd chiari syndrome (1)) were included into the study. Bile fluids were obtained by ERC. After extraction of genomic DNA, a mutation "enriched" PCR-RFLP was performed. If K-Ras mutations were detected by a second band in gel electrophoresis, the PCR products were subcloned and DNA sequencing was performed.

Results: None of the 19 patients with benign cholestatic liver diseases