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data from a population-based cancer registry. Information on octogenarians and nonagenarians who underwent resection for gastric cancer or colorectal cancer in the period 1987-2000 was retrieved from the Rotterdam Cancer Registry. Postoperative mortality was defined as death within 30 days of operation and proportions were tabulated by turnour site and age-group. Differences between subgroups were evaluated with chi-square testing. This study comprises 2765 patients with colorectal cancer and 424 patients with gastric cancer. For colorectal cancer, postoperative mortality rates increased from 8% in patients aged 80 to 84 years, to 13% in patients aged 85 to 89 years and to 20% in nonagenarians (p

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## Increased bone marrow-derived endothelial cells in Barrett's metaplasia

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Background: Barrett's metaplasia represents the first step in a metaplasia-dysplasia-adenocarcinoma sequence. Oesophageal adenocarcinoma is characterized by early vascular invasion and metastasis. Circulating endothelial progenitor cells (EPCs) differentiate into mature endothelial cells in areas of injury and are involved in vasculogenesis and tissue repair. It is reported that these EPCs are mobilized from the bone marrow by various growth factors and cytokines including VEGF and IGF-1. We hypothesized that, circulating progenitor endothelial cells are upregulated in Barrett's metaplasia in response to elevated levels of serum VEGF and/or IGF-1.

**Methods:** Three groups of patients were studied. Group 1 (n=10) were normal controls; Group 2 (n=15) had benign reflux disease; Group 3(n=20) had Barrett's metaplasia. Fresh blood was analysed via flow cytometry using a panel of 3 antibodies: CD146, CD133 and CD45. Serum VEGF and IGF-1 was measure via ELISA. Data was analysed using ANOVA, LSD post-hoc statistics (SPSS software).

**Results:** EPCs were significantly increased in patients with Barrett's metaplasia (3.77  $\pm$  0.89) versus benign reflux (1.4  $\pm$  0.4) or controls (0.75  $\pm$  0.41) (p<0.5). Circulating endothelial cells levels was greatest in Barrett's metaplasia but this increase was not significant (3.33  $\pm$  1.04 vs. 1.9  $\pm$  0.5 vs. 2  $\pm$  0.46). Serum levels of VEGF and IGF-1 did not differ significantly between the patient groups.

Conclusion: Circulating progenitor cells but not mature endothelial cells were increased in Barrett's metaplasia. Since progenitor cells are provasculogenic they may contribute to tumourigenesis and early microvascular invasion in Barrett's adenocarcinoma.

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## Oxaliplatin plus capecitabine in advanced biliary adenocarcinomas: a multicenter phase II trial

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**Background:** At present, no standard chemotherapy is established for the treatment of advanced adenocarcinomas of the biliary system. Therefore, we determined the efficacy and safety of oxaliplatin combined with capecitabine in patients (pts) with unresectable or metastatic gallbladder carcinoma (GBC) or intra-/ extrahepatic cholangiocarcinoma (CCC).

Material and methods: 41 pts (19M, 22F) were included. Median age was 63 yrs (range 28-74). Major eligibility: histologic proven, measurable disease, age ≤ 75 yrs, ECOG PS ≤2. A total number of 126 cycles (median: 5; range 1-11) of combined oxaliplatin (130 mg/m², d1) and capecitabine (2000 mg/m², d 1-14), were administered every 3 weeks for advanced GBC (14 pts), intrahepatic (12 pts) and extrahepatic CCC (15 pts). Pts were assessed for response according to WHO standard criteria initially after 2 cycles, thereafter every 3 cycles. Results: On 24 evaluable pts, 6 (25%) partial responses (PR) were observed; 14 pts (58%) had stable disease (NC); progressive disease (PD) was diagnosed in 4 pts (17%). Median overall survival and median time to progression were not reached. Grade 4

toxicities (WHO) were diarrhea in 1 pt (1% of cycles), peripheral sensory neuropathy in 2 pts (2%), and fever in 1 pt (1%); grade 3 toxicities were: diarrhea in 2 pts (2% of cycles), thrombocytopenia in 2 pts (4%), fever in 1 pt (1%), peripheral sensory neuropathy in 5 pts (12%). One patient was removed from study after six courses for an allergic reaction to oxaliplatin.

Conclusions: This phase II study demonstrates that an outpatient protocol of oxaliplatin plus capecitabine for advanced biliary tract adenocarcinomas is highly active (disease control rate: 83%) and well tolerated. Updated results will be presented at the meeting.

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Outcomes in patients with metastatic colorectal cancer (MCRC) treated with infusional cpt-11/5fu/leucovorin (CFL)under a stringent positive-response dependent protocol: less treatment does not compromise outcome

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Background: CPT-11/5FU/leucovorin (CFL) has recently become the new reference regimen in patients with metastatic colorectal cancer (MCRC). However, the optimal duration of therapy with CFL in MCRC is not well defined and many experts recommend continuous treatment until disease progression or intolerance. We designed a study to examine 1) the efficacy of CFL in Chinese patients in the first-line setting 2) the impact on survival outcomes by limiting continuation of therapy only to patients with a positive response.

Material and methods: Between 8/2000 and 7/2001, 67 consecutive patients with MCRC and adequate haematological and renal/hepatic functions entered the study conducted in two affiliated institutions. Median age: 56, median ECOG: 0. Previous adjuvant chemotherapy: 30%. No. of organs/sites involved: 1-3 (median 2). Liver metastases: 71.6%. Regimen: fortnightly cycles of CFL: CPT-11 180mg/m2 q2h infusion D1, Leucovorin 200mg/m2 q2h D1+2, 5FU 400mg/m2 bolus/600mg/m2 q20hr infusion D1+2. Imaging evaluation (all CT) was performed after every 4 cycles and continuation of therapy was strictly response-dependent: PD after 4 cycles: stop chemotherapy; SD/PR/CR after 4 cycles: proceed to 8 (stop at 8 if CR after 4); PD/SD after 8 cycles: stop chemotherapy; PR/CR after 8 cycles: proceed to 12 (stop at 12 if CR after 8); PD/SD after 12 cycles: stop chemotherapy; PR/CR after 12 cycles: proceed to 16 (stop at 16 if CR after 12); PD/SD after 16 cycles: stop chemotherapy. No patients will receive >16 cycles regardless of their response status Response status was determined by comparing the latest imaging with the last CT, not the baseline CT, except for after the 4th cycle.

Results: 592 cycles of CFL were given. Median follow-up: 15months(m). Median no of cycles: 8. Median duration of treatment:18.4 weeks(w). Dose intensity of CPT-11: 96% and full-dose cycles in 92% of cycles. 62 pts evaluable for response (with >/=4cycles given). Response: Not Evaluable:7.5%, PD:15%, SD:34.3%, PR:34.3%, CR:8.95%. Median duration of response: 11.1m. Median progression-free survival: 9.2m. Median OS: 15.5m. 67 pts were evaluable for toxicities. Grade \* neutropenia: 22% of cycles, fever: 1.8% of cycles, neutropenic fever: 7.5% pts and 0.8% of cycles and admission required in 3 pts. Diarrhea of any grade: 15.5% cycles and 64.2% pts. No G3/4 diarrhea but imodium use observed in 10.1% of cycles. Nausea/vomiting: all G1/2 and in 73% of pts and 49.3% of cycles. Salvage chemotherapy (mostly with oxaliplatin) given in 37.3% pts.

Conclusions: Compared with large international studies using first-line CFL in MCRC, the present regimen achieved comparable endpoints, especially in OS, with a shorter duration of treatment (e.g. 24.6w, Douillard et al, Lancet 2000; 23.8w Saltz et al, NEJM 2000). This response-dependent policy may have both economic and quality-of-life implications and further studies are warranted to further define the optimal treatment duration of CFI