administered at 500 mg (highest safe dose from Part 1) with 5-FU/LV between days 8-12 (cycle I) and days 36-40 (cycle 2). Dose-limiting toxicity (DLT) up to 56 days was defined as the occurrence of drug-related: G3/4 neutrophil or platelet toxicity (>7 days duration); febrile neutropenia; G3/4 skin rash; G3/4 diarrhea, nausea or vomiting (>4 days duration) despite standard supportive measures; significant ocular toxicity; or occurrence of other G3/4 major end organ toxicity. One-hundred and thirty courses have been delivered in Parts 1 (117) and 2 (13), respectively, and DLT has not been observed to date. GI/2 adverse events (AEs) reported included rash, diarrhea, mucositis and neutropenia. G3/4 AEs included neutropenia and G3 diarrhea in 1 pt. No apparent increased frequency or severity of diarrhea or skin toxicity beyond that seen with 5-FU/LV alone was observed. In addition, there was no evidence of cumulative toxicity or emergence of new or unusual toxicity with continued exposure. No significant drug-drug interactions have been observed following preliminary PK analysis of ZD1839 and 5-FU exposure at 250 mg I-ZD1839. At day 56, after two 5-FU/LV courses and 2 wks ZD1839, I complete and 4 partial responses (3 confirmed) have been observed on the I-ZD1839 schedule. Thus, the combination of ZD1839 and 5-FU/LV is feasible and has a manageable safety profile.

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## A phase II study of gemcitabine and oxaliplatin (gemox) in advanced billary adenocarcinoma (ABA). Preliminary results

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Pre-clinical data support an optimal synergistic effect using the sequence gemcitabine followed by oxaliplatin (Faivre S, Cancer Chemother Pharmacol 1999, 44(2):117-23). Based on the results of the gemcitabine oxaliplatin combination in advanced pancreatic adenocarcinoma (Louvet C, Proc Am Clin Oncol 2001; 20), we designed a phase II, to determine activity and tolerance of this combination in ABA. Since July 2000, twenty two eligible patients (pts) received the GEMOX regimen: GEMcitabine 1000 mg/m* in 10mg/m*/mn infusion D1, OXaliplatin 100 mg/m* in 2h infusion D2; treatment was repeated every 2 weeks until progression of disease or limiting toxicity. Eligibility criteria were pathologically-proven biliary adenocarcinoma, PS (ECOG) 0-3, age 18 to 80 yrs, adequate hematological, renal and liver functions, measurable disease, control of pain and jaundice before inclusion, and written informed consent. Pts characteristics: 12 male/10 female; mean age 70 yrs, range 40-80; PS: 0 = 7, 1 = 9, 2 = 5, 3 = 1; 2 Locally Advanced (LA)/20 Metastatic (M); chemotherapy line: 1 = 19, 2 = 2, 3 =1; tumor sites: gallbladder 8, extrahepatic bile ducts 3, ampula of vater 3, intrahepatic bile ducts 7, unknown 1; M tumor sites: liver = 16, lung = 3, distant lymph nodes = 2, peritoneum = 4. Toxicity: 139 cycles were administered (median 5, range 1-18). No NCI CTC grade 4 was observed. Grade 3 (% cycle/% of pts): neutropenia 0.7%/4.8%, thrombocytopenia 0.7%/4.8%, nausea-vomiting and diarrhea 0%/0%; grade 2 alopecia 9.5%, grade 3 peripheral neurotoxicity (specific scale) 4.8% of pts. Overall, 14.3% of pts experienced a grade 3 toxicity. Efficacy: (investigators) 5 PR, 3 SD, 6 PD and 8 to early were observed for a response rate (WHO criteria) of 35.7% (5pts/14).

**Conclusion:** GEMOX combination is active and well tolerated in ABA. Accrual continues to this study. Updated data with progression free survival and overall survival will be presented at the meeting.

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## Partial duodenopancreatectomy with radical lymphadenectomy in patients with pancreatic carcinoma

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**Purpose:** Partial duodenopancreatectomy (PD) is the treatment of choice for carcinoma of the pancreatic head and periampullary carcinoma. In contrast the benefit of radical lymphadenectomy in these patients is still discussed controversially.

**Methods:** 117 patients with ductal adenocarcinoma of the pancreas who underwent PD between 1988 and 2000 and received either a regional lymphadenectomy (Group A) or an extended radical lymphadenectomy (Group B) were included in survival studies according to Kaplan-Meier. 52 male and 65 female patients with an median age of 62 years were analysed.

**Results:** Perioperative mortality was 4.3% (5 pat.). The stage distribution according to the UICC was: Stage I: 8 (6.8%), stage II: 23 (19.7%) stage III: 58 (49.6%), Stage IVa+b: 28 (23.9%). Overall 5-year survival rate of these patient was 18%. 5-year survival of curative (R0) resected patients was 23%.

A significant difference could be observed in these group between patients with negative lymph node status (36% 5-year survival) and positive lymph node status (17% 5-year survival). Whether no significant difference could be observed between patients in Group A or B. If only early UICC-tumor stages were compared patients in Group B seemed to have a benefit in survival compared to group A.

**Conclusion:** The data indicate that extensive retroperitoneal tissue clearance for ductal adenocarcinoma does not improve overall survival compared to regional lymphadenectomy. Patients with early tumor stages might benefit from the extended approach.

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## Intra-arterial hepatic chemotherapy with oxaliplatin combined to intravenous treatment with 5FU + folinic acid in hepatic metastases of colorectal cancer

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**Purpose:** Due to increase of tumoural exposure to the drugs, intra-arterial hepatic chemotherapy (IAHC) increases response to chemotherapy when fluoropyrimidines (5FU or FUDR) are used. With new drugs such as oxaliplatin and irinotecan the interest of this sometimes difficult way of therapy has been debated. We tried to use one new drug, oxaliplatin, administered intra-arterially in order to increase response rate and to decrease systemic toxicity.

**Methods:** From May 1999 to January 2001, 23 patients with isolated hepatic metastases of colorectal cancer were included in a phase II study. Patients could have received one previous treatment combining 5FU + folinic acid for their metastatic disease. They should have adequate bone marrow function and adequate liver, cardiac and renal functions. Study protocol: every two weeks the patients received: oxaliplatin 100 mg/m2 IAH 2-hour infusion + FA 200 mg/m2 2-hour infusion i.v. followed by 5FU 400 mg/m2 i.v. bolus followed by 600 mg/m2 as continuous infusion for 22 hours day 1, FA and 5FU were repeated day 2.

**Results:** 14 men, 19 women, median age: 59 years [44-72]. The median percent of liver involvement was 30% [10-60%]. Median number of cycles was 6 [1-20]. Treatment was stopped in 15 patients (pts): for progressive disease: 2 pts, obstruction of the catheter: 9 pts, other reason: 4 pts. Toxicity was frequent but mild. Grade 3-4 leucopenia: 4 pts, neutropenia: 7 pts, thrombopenia: 1 pt. There was one toxic death due to a neutropenic sepsis. Response rate in 14 evaluable patients (7 too early, 2 less than 4 cycles due to early catheter obstruction): complete response: 1 pt, partial responses: 10 pts, stable disease: 3 pts; objective response rate: 79%. Three patients underwent complete resection of their metastases after response to IAHC. Six-month survival was 86% [66%-95%].

**Conclusion:** this combined hepatic arterial with oxaliplatin and systemic chemotherapy allowed to observe very high response rate with manageable toxicity.

# Lung cancer 1

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## Randomised phase II study of BMS-275291 versus placebo in patients (pts) with stage IIIb or IV non small cell lung cancer (NSCLC) receiving paclitaxel + carboplatin (PC): National Cancer Institute of Canada Clinical Trials Group (NCIC CTG) br.18

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BMS-275291 is a novel matrix metalloprotease inhibitor (MMPI) with broad activity against MMPs but without the dose limiting arthrotoxicity seen with BB2516 (marimastat) and AG3340 (prinomastat). The objective of the phase II study was to determine the incidence of arthrotoxicity and other toxicities, as well as to examine whether the objective response rate for either arm was in keeping with that expected for PC based upon review