intraperitoneal chemotherapy. Mean operative times was 323 minutes, and mean blood loss were 1 207 milliliters. There was no mortality. Morbidity was related to four transient biliary leakages. There was no systemic complication due to chemotherapy. Hospital stay was 22 days. After a median follow-up of 14.4 months, there was no detectable recurrence of the peritoneal carcinomatosis. At the end of the study, seven patients were disease free. When minimal or moderate peritoneal carcinomatosis is detected during hepatic metastasectomy, the association of a hepatectomy with complete cytoreductive surgery of peritoneal carcinomatosis immediately followed by intraperitoneal postoperative chemotherapy is logical, and safe. This agressive treatment is well tolerated, although the frequency of biliary leakages is higher than after standard hepatectomy. Absence of peritoneal recurrence, and rate of survival are promising.

744 POSTER

Biological factors predicting the outcome of regional chemotherapy in colorectal carcinoma metastases to liver

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Purpose: Regional intrahepatic chemotherapy may be beneficial for selected subgroup of patients with liver metastases of colorectal carcinoma. However, biological criteria precising indications to this demanding type of treatment have not yet been established.

Methods: Twenty two cases of colorectal carcinoma metastases to liver treated by regional chemotherapy were analysed for DNA ploidy and PCNA, Ki67, p53, p21 (WAF1), mdm2, c-erb2, CEA, CA19-9 and P-glycoprotein (MDR) expression and results related to survival.

Results: Mean survival of patients with DNA diploid tumors was significantly longer (20 versus 11 months, P = 0.04) comparing to DNA aneuploid ones. Only the trend for lower PCNA positivity and p53 expression could be observed among DNA diploid tumors. All p53 positive cases were negative for p21 (WAF1) and mdm2. Other parameters were unrelated to outcome of treatment.

Conclusion: DNA ploidy, perhaps together with p53 overexpression and PCNA positivity, may be predictive of effectiveness of regional intrahepatic chemotherapy performed for colorectal cancer liver metastases. However, a larger study is needed to confirm these preliminary findings. (Supported by IGA MZ CR grant No.2923-3)

745 POSTER

Infusional 5-fluorouracil with and without calcium-folinat as second line therapy in advanced colorectal cancer – A retrospective cohort study of different protracted infusion regimens

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Purpose: Biomodulation of 5-Fluorouracil (5-FU) with Calciumfolinat (CF) in bolus regimens increases response rates, and probably survival rates of patients with advanced colorectal cancer (CRC). The benefit of CF in second line protracted infusional protocols of 5-FU is not so clearly defined. Consequently we compared the outcome of two infusional 5-FU regimens with and without CF.

Methods: Fifty-eight patients with CRC were treated from May 1991 until September 1996 with two different second line infusional 5-FU protocols after failure of CF-modulated 5-FU – bolus regimens (380–450 mg/m^2 5-FU + 20–200 mg/m^2 CF d1–5 q 4w). Twenty-eight patients received 60 mg/kg 5-FU alone as a 48 hours infusion with ambulatory pumps every week until progression. Thirty patients were treated with 500 mg/m^2 CF as a 2 hours infusion followed by 2600 mg/m^2 5-FU as a 24 hours infusion every week with a third weeks rest until progression. Kaplan-Meier survival analysis and the log-rank-test were applied.

Results: The two cohorts were adequately matched in respect of age, tumor load, and time to progression after first line therapy, and received a mean of 27 resp. 14 cycles. The CF-scheme exhibits higher response rates but more toxicity. Median survival times (30 resp. 46 months) were significantly different (p = 0.09).

Conclusions: CF modulation of 5-FU in protracted infusional protocols as second line therapy increases response rates and survival rates of CRC patients.

746 POSTER

Oxaliplatin (LOHP) and 5-fluorouracil (5-FU) synergism in advanced colorectal cancer patients (ACRC)

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Previous in vitro and in vivo studies reported LOHP and 5-FU synergistic effect in ACRC. We studied their combination in 5-FU refractory ACRC. **Pts and Methods:** pts had high dose 5-FU-folinic acid (FA) refractory ACRC (progressive disease while on 5-FU-LV treatment). LOHP was added, at 130 mg/m^2/3 weeks by IV infusion over 2 hours, to unchanged 5FU-LV schedule, 1.3 g/m^2 weekly 5-FU, plus 400 mg/m^2 FA.

Results: 38 patients from 6/94 to 5/96, with measurable disease in all pts. Mean age: 64; PS: 0 (15), 1 (15), 2 (7), 3 (1), sites involved: liver: 27, lung: 7, peritoneum carcinomatosis with measurable mass: 10, lymphnode: 1, number of sites involved: 1 site: 26, 2 sites or more: 12; previous radiotherapy: 9; mean duration of 5-FU-LV-LOHP: 4 cycles (1 to 12). WHO toxicity was: neuropathy: 56 GI, 15 GII, in 22 pts; neutropenia: 10 GI, 4 GII, 2 GIII in 7 pts; thrombopenia: 8 GI, 6 GII, 4 GIII in 8 pts; diarrhea 15 GI, 18 GII, 6 GIII in 14 pts; 8 pts (21%) had grade III toxicity. Responses (WHO): 14 PR (36%), 14 SD, and 10 PD after 3 cycles of LOHP-based treatment; mean duration of the response: 6 mths (1 to 11), median Progression Free Survival: 5.5 mths, median Overall Survival: 7.6 mths, 9 pts were alive at +12 mths.

Discussion: LOHP-5-FU-LV have synergistic activity; toxicity is mild; response rate appears to be higher than expected with LOHP alone in 5-FU refractory ACRC. This combination merits further investigation in first line chemotherapy.

747 POSTER

Biweekly administration of methotrexate (MTX), levofolinic acid (LFA), and 5-fluorouracil (5-FU) in advanced colorectal carcinomas

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Background: In a previous phase II study, 54 colorectal cancer patients (pts) received biweekly MTX (500 mg/m^2) 24 h before 5-FU (600 mg/m^2) + LFA (250 mg/m^2) administration. A 26% ORR was observed in chemo-naive pts.

Purpose: To test whether higher MTX and 5-FU doses could improve the ORR without increasing the acute toxicity.

Methods: Patients with advanced colorectal cancer received MTX 750 mg/m^2 on d 1 followed 24 h later by 5-FU 800 mg/sqm and LFA 250 mg/m^2 every 2 weeks until PD or for a maximun of 16 courses.

Results: As of Jan 97, 100 pts were enrolled and 90 pts (48 chemo-naive, 42 pretreated) were evaluable for response (10 pts were too early), according to intention-to-treat analysis. Overall, 25 pts achieved a response: 19/48 (40%, 95%CI = 26–55) chemo-naive and 6/42 (14%, 95%CI = 5–29) pretreated pts. Toxicity: the treatment was usually well tolerated, but 3 treatment-related deaths and 4 early withdrawals for toxicity occurred. Only 2/7 of these events were observed in chemo-naive pts. Grade 3–4 mucositis and diarrhoea occurred in 12% and 9% of courses, respectively, and were less frequent in chemo-naive pts. Grade 4 neutropenia and thrombocytopenia each occurred in less than 5% of courses.

Conclusions: The biweekly administration of MTX followed by 5-FU+LFA is a well tolerated treatment for colorectal cancer pts and it shows a very interesting activity both in chemo-naive and pretreated pts.

748 POSTER

Insulin-like growth factor binding protein-3 (IGFBP-3) proteolysis in patients with colorectal cancer: A possible early prognostic factor of metastatic progression

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Purpose: The Insulin-like Growth Factor (IGF) system plays a key role in intestinal epithelial cell functions and colorectal neoplastic growth. In human,