3 per day versus (A) 100 mg × 3 + (L) 4 mg × 3 per day. Sixty-two patients with advanced colorectal cancer refractory to 5 FU received CPT 11 at the dose of 350 mg/m^2 every 3 weeks. Only 27 are so far evaluable. However is too early to draw any conclusion. Final result will be presented.

760 PUBLICATION

METHOTREXATE (MTX) AND 5-FLUOROURACIL (5-FU) IN ADVANCED COLORECTAL CANCER PATIENTS PREVIOUSLY TREATED WITH ADJUVANT 5-FU

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5-FU cytotoxicity may be increased through biochemical modulation with MTX. This can be important in patients who have already received 5-FU in the adjuvant setting. We have employed a combination regimen of MTX followed by 5-FU, with leucovorin (LV) rescue, in a series of patients with advanced disease. Pts were required to have symptomatic, measurable, inoperable lesions from colorectal cancer, recurring after adequate radical surgery of the primary tumor and adjuvant 5-FU + LV, concluded at least 3 months before recurrence. Pts received MTX, 250 mg/m^2 as a 2-hours i.v. infusion, followed by two doses of 5-FU, 500 mg/m^2 as i.v. bolus 1 hour and 21 hours after the end of methotrexate infusion. LV rescue, 15 mg orally every six hours for 7 times, was started 1 hour after the second 5-FU dose. The cycle was repeated every 2 weeks.

Results: Twenty-two pts entered the trial, and 21 were evaluable. An objective response was observed in one pt (4.8%), 7 pts (33.3%) obtained tumor regression < 50% or disease stabilization. Thirteen pts (61.9%) progressed. Median survival in the whole group was 11 months. Toxicity was mild.

Conclusions: biochemical modulation with MTX does not seem a satisfactory mean to increase 5-FU activity, when the patient has been previously exposed to 5-FU plus LV.

761 PUBLICATION

CURATIVE SURGERY IN METASTATIC OR RECURRENT COLON CANCER

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Twenty-eight pts with recurrent or metastatic colon cancer underwent radical resection of disease with curative intent. 16 were male and 12 female. The mean age was 65 years (median 68, 38–84). 4 pts had stage B1, 8 had B2, 2 had stage C1, 4 C2 and 10 had stage D at presentation according to Astler-Coller staging system. In 8 pts local recurrence was resected, in 15 surgery was performed for liver metastases (8 at diagnosis and 7 for recurrences), in 3 lung secondaries were resected and in 2 pts Krukenberg tumors of the ovaries were removed at first operation. The median time interval from diagnosis to surgery was 13 months (mean 16, 0–85). 11/28 pts (40%) are alive with no evidence of disease, 7–66 months from surgery (2 local recurrence, 6 liver metastases and 3 lung secondaries).

Conclusion: Curative radical resection in recurrent or metastatic colon carcinoma can produce long term disease free survival in a selective group of patients.

762 PUBLICATION

MORPHOLOGIC FEATURES AND ASSESSMENT OF CARCINOMAS RISK DEVELOPMENT IN PATIENTS WITH COLORECTAL ADENOMAS

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The clinical significance of colorectal polyps emerges from the adenoma-carcinoma sequence theory. This theory includes size-dependent risk of malignancy in adenomas and a failure to find minute, "de novo" carcinomas surrounded only by normal mucosa. The retrospective study was carried out on 141 colorectal adenomas diagnosed in 94 patients; male to female ratio 2.35:1. Polyps were obtained by endoscopic polypectomy performed during the total colonoscopy. Most adenomas were located in the sigmoid colon and the rectum, and the percentage decreased proximally to the right colon. Histological examination revealed that, among 141 adenomatous polyps, there were 122 (86.52%) tubular, 12 (8.51%) tubulovillous and 7 (4.96%) villous adenomas. The epithelial dysplasia was graded as mild in 57 (40.42%) adenomas, moderate in 44 (31.20%) and severe in 6 (4.25%). Invasive carcinoma was observed in 11 (7.80%), while 23 (16.31%) adenomas were without dysplasia. The percentage of severe dysplasia was greater in villous than in tubular adenomas ($P < 0.01$) and correlated with the increasing size of the adenomas ($P < 0.01$). There were no complications during endoscopic polypectomy. Follow-up over 6–24 months revealed no recurrences in any case.

763 PUBLICATION

CONTINUOUS LOW DOSE, ORAL DOXIFLURIDINE (DFURD, 5'-DEOXY-5-FLUOROURIDINE) FOR THE GENERATION OF NON-TOXIC 5FU LEVELS IN COLORECTAL CANCER

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Fluoropyrimidines are one of the few treatment options for colerectal cancer. We describe the use of oral dFUrd (a 5FU prodrug) administration in order to generate low, stable 5FU concentrations and to avoid toxic side-effects. dFUrd (D = 600–1000 mg/m^2) was given to 6 colerectal patients. Daily doses resulted in continuous systemic levels between 1–5 μg/ml which could be maintained during several weeks without any side-effects at all. The biovailability was 32–45%. Renal excretion (3.2–46%) was dose dependent and related with changes of 5FU metabolism. One patient had a partial remission and one a stable disease at 1000 mg/m^2, illustrating the known activity of fluoropyrimidines in the treatment of colerectal cancers. It is concluded that continuous, low dose oral dFUrd results in continuous, non-toxic levels of dFUrd up to 5 μg/ml for several days. These findings are supplementary to the sensitizing influence of ras (frequently mutated in colerectal cancer) for dFUrd activity.[1] But also the possible drag carrier function of dFUrd (enhanced anthracycline uptake in cell lines after dFUrd exposure, non-related to multidrug resistance) makes the further study of continuous, low dose oral dFUrd administration warranted as non-toxic (adjuvant) treatment for colerectal cancer.[2]

1. Y. Geng, *et al. Biochem Pharmacol1991 41,303.*2. S. van den Heyden, *et al. Jpn J Cancer Res* 1994 **85**,13.