this disease and the combination with CPT 11 is therefore a priority. Adding these two non-cross-resistant drugs without overlaping toxicities was the rationale of this alternating schedule. **Treatment Schedule:** CPT11· 350 mg/m^2 iv, 90 mn (day 1) and 5 FU. 425 mg/m^2 iv 15 mn, immediately after FA 20 mg/m^2 iv push, daily times 5 (d22 to d26) every 6 weeks.

Population: Pts with metastatic CRC and bidimensionally measurable lesions, no prior CT or only adjuvant regimen ended more than 6 months before study entry. Age. 18–70 years, PS ≤ 2; adequate hematological, renal and hepatic functions Tumor assessment is performed every 2 single cycles.

Results: 33 pts have been treated· 18 men (55%), 15 women (45%), 17 colon (52%), 13 rectum (39%), 3 rectosigmoid (9%), 15 PS = 0 (45%), 18 PS = 1 (55%). Preliminary efficacy results (after at least 2 single cycles completed) reviewed by External Response Review Committee among 29 evaluable patients show: 9 PR, 4 MR, 13 SD and 3 PD. Out of 133 performed single cycles, 22 (16%) have been delayed (14 CPT11 cycles and 8 5 FU cycles) and 11 cycles (8.3%) have been performed with those reduced (8 CPT11 cycles and 3 5 FU cycles). **Toxicity:** (>WHO grade 2): preliminary results on 30 evaluable patients are neutropenia (6 pts – 20%), febrile neutropenia (4 pts – 13%), vomiting (2 pts – 70%), diarrhea (6 pts – 20%), mucositis (3 pts – 10%) and cholinergic syndrome (1 pt – 3.3%).

Conclusion: These preliminary results indicate that an alternating schedule of CPT11 and 5 FU/FA is feasible and that the antitumor activity is promising in metastatic CRC.

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Phase II study of 24 hours-infusion of 5-fluorouracil and high dose folinic acid in patients with progressive or recurrent colorectal cancer (CRC)

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Purpose: To evaluate the therapeutic activity of 24 h continuously infused 5-FU modulated by HD-folinic acid (FA) in pts with metastatic CRC who had recurred or progressed following bolus 5-FU based chemotherapy (CTX).

Patients and Methods: 42 pts, 27 men and 15 women with a median age of 59 years (45–76), were enrolled. Karnofsky status: 90% (80–100); previous CTX regimens. bolus 5-FU/FA acid n = 31 (74%), c.i. 5-FU ± IFN-α2 n = 9 (21%), other n = 2 (4%). Treatment schedule: 500 mg/m^2 FA given as 2-h infusion followed by a 24 h infusion of 2 6 g/m^2 5-FU once weekly × 6 (i.v.).

Results: All pts were assessable for toxicity and for response evaluation having completed at least 1 full course of ctx. No CR but 6 PR were observed [ORR, 14% ($CI_{95\%}$: 3.5–25.1%)]. The median response duration was 7.3 mon (1.4–10.6), median survival 11.6 mon [2–27 ($CI_{95\%}$: 9.4–13.8)] and the 1-year-survival rate 46%. SD/MR were achieved in another 25 pts (61%). Median treatment duration was 19 weeks (range, 6–48). WHO °III/IV diarrhea occurred in 26%, mucositis, nausea/vomiting and hand-foot-syndrome in 5% each of patients. No severe infection/fever or evidence of hematological toxicity was observed, except WHO °III anemia and leukocytopenia (each 5%). Dose reductions in 11 pts and subsequent stop of treatment in 2 pts had to be performed because of unacceptable diarrhea. PD while receiving previous ctx was associated with lower response rate (p = 0.02), shorter PFI (p = 0.02) and survival (p = 0.01) as compared to the subset of pts who achieved temporary SD.

Conclusion: C.i. infusion of 5-FU/FA displays activity in advanced CRC with toxicity being acceptable. Pts who had achieved at least SD during previous bolus 5-FU based CTX appear to benefit from second-line continuously infused 5-FU/FA. Questions remaining to be addressed in order to optimize the approach include (1) the optimal start dose of 5-FU (2) whether FA can be reduced or eliminated to achieve a better toxicity profile and lower costs.

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Quality of life (QL) is a prognostic factor (PF) for survival in patients with advanced colorectal cancer (CRC)

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Recent years have seen a discussion on which group of patients should be offered chemotherapy for advanced CRC regarding the limited efficacy and high costs of treatment and its' possible side effects on patients' QL. In a randomized phase III trial, 142 patients with advanced CRC were treated with 5-fluorouracil and either interferon α-2b or folinic acid. For the QL self-assessment before and during chemotherapy, a major end point of the study, patients used the validated EORTC QLQ-C30 questionnaire, which consists of 5 functional scales (physical state, ability to work, and cognitive, emotional and social state), 9 symptom scales (pain, nausea, vomiting, fatigue, dyspnea, loss of appetite, sleep disturbances, diarrhea, and constipation), and one global QL scale. Next to the above 15 QL scales we tested 20 covariates for their relevance as PF and survival. In univariate analysis, response to therapy, performance status (PS), appetite loss, physical, emotional, and role function as well as AP, SGOT, SGPT, and WBC had a significant impact on survival. However verifying the influence of these variables on survival in a multivariate setting reduced the number of significant prognostic factors to only three: a Karnofsky PS > 70% (p = 0.003), little or no loss of appetite (p = 0.003), and a WBC < 10.000 (p < 0.001). A classification including these three PF was able to distinguish between low-risk patients, who survived a median of 12 months, and high-risk patients, who had a median survival time of only 3 months. Therefore, this prognostic classification can facilitate the decision whether patients with advanced CRC should be considered for systemic chemotherapy

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Orthotopic transplantation of intact human colorectal and pancreatic tumor tissue in nude mice

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Purpose: A relevant model of human gastrointestinal cancer in nude mice will improve our understanding of carcinogenesis and cancer metastasis.

Methods: We have established an orthotopic transplantation model in nude mice with intact tissues of human colorectal and pancreatic cancers. The biological characteristics of the original and the corresponding transplanted tumors were investigated by HE staining, PAS staining and immunostaining.

Results: (1). There were totally 9 of 16 surgical specimens growing in nude mice subcutaneously and/or orthotopically (4/6 colon and 5/10 pancreatic cancer). Freezing of tissue specimens and tumor cell content of the specimens influenced the take rate of transplanted tumor. In the group of fresh tumor tissues with greater than 50% tumor cell content, the take rate was 100% (3/3 pancreatic and 3/3 colon). (2). The transplanted tumor closely resemble the original tumor morphologically and biologically, including TAA expression such as CEA by immunostaining, and CEA level in the serum of mice. (3). The detection of dissemination of cancer cells can be achieved by immunostaining. (4). Antigen expression of Ki-67, K-ras, 17-1A and RA-96 were associated with the potential of tumor growth in nude mice.

Conclusion: An orthotopic transplantation model and a sensitive detection method for human colon and pancreatic cancer in nude mice were established. This study will be helpful for monitoring therapeutic intervention strategies for micrometastatic disease.

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MRI and endoluminal ultrasound result in different staging in 5 out of 17 patients with anal cancer

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Purpose: In cancer of the analcanal endoluminal ultrasound (US) is the staging modality of choice. Treatment of choice is chemoradiotherapy. Accurate staging is extremely important as many clinicians treat patients with T1/2 tumors with a lower dose of RT and CT than in T3/4 tumors. Because there are no data available in the literature we investigated the role of MRI in the staging of analcanal cancer and compared it with endoluminal US.

Methods: 17 patients underwent both, MRI with a body coil and US. Tumor stage by US was the following: uT1 (<2 cm): 3; uT2 (2–5 cm): 9; uT3 (>5 cm): 3 and uT4: 2. Positive lymph nodes were seen in 4 patients.

Results: In 5 out of 17 patients (30%) a higher stage was seen using MRI. In three cases the stage was changed from T1/2 up to T3 and therefore