a lower rectum adenocarcinoma. 4 with an anal epidermoid, and 2 with a primitive anorectal melanoma. All patients with an adenocarcinoma had post-operative radiotherapy. Preoperative evaluation, surgical technique, and postoperative care are described.

Results: No deaths occurred in the postoperative period. Nine patients had a perineal separation, one distal colic necrosis and one neorectal perforation by irrigation necessitating an iliac colostomy on days 14 and 21. Two patients had to undergo anal dilatation. Three mucous prolapses and 2 perineal eventrations, all late occurrences, complete the list of complications. Functional results were evaluated with Kirwan's classification: 4 patients had normal continence, 24 gas incontinence, 10 occasional minimal soiling, and 2 cases necessitated a left iliac colostomy.

Conclusion: Peudocontinent perineal colostomy following abdominoperineal resection is a safe reconstruction technique which provides good functional results following strict selection of patients.

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A phase II-study on intense weekly 24-hour intraarterial infusion with 5-fluorouracil (5-FU) and folinic acid (FA) for colorectal liver metastases

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Purpose: The aim of this phase II-study was to demonstrate the toxicity and the improved response rates of weekly 24-h hepatic arterial infusion (HAI) of 5-FU and FA for unresectable liver metastases from colorectal carcinoma.

Methods: In 26 patients (15 male, 11 female), 268 courses of high-dose HAI of 5-FU/FA were administered. The chemotherapy regimen consisted of a weekly HAI of FA 500 mg/sqm over 2 h, immediately followed by HAI of 5-FU over 24 h. 14 patients received a 5-FU starting-dose of 2600 mg/sqm, 4 patients of 2400 mg/sqm and 8 patients of 2200 mg/sqm. One course consisted of 6 weekly applications followed by a two week break.

Results: The applied regimen caused only a low rate of clinical relevant side effects. Diarrhea was most frequently seen with 15 episodes WHO-grade $\geq$3 out of 268 courses. Nausea and vomiting were a minor problem occurring with 3 episodes WHO-grade $\geq$3. There was no evidence of myelosuppression, neurotoxicity and biliary sclerosis. 53 applications (19.7%) were without any side effects. A partial remission was observed in 20 (77%) patients, and a disease stabilization in 4 (15%) patients while the disease progressed in 2 (8%) patients.

Conclusion: The present phase II-study demonstrates that the weekly high-dose HAI of 5-FU/FA was well tolerated despite the dose limiting diarrhea. Because of this extraordinary high response rates without local hepatobiliary toxicity this regimen should be used for further randomized trials comparing intraarterial versus intravenous therapy.

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A phase II trial of trimetrexate (TMTX), 5-fluorouracil (5-FU) and folinic acid (FA) in untreated patients with advanced colorectal carcinoma

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Purpose: TMTX is a non-classical antifolate and has been shown to increase the activity of 5-FU and FA. We evaluated the safety and efficacy of TMTX, 5-FU and FA in patients with metastatic colorectal cancer.

Methods: 34 patients were enrolled into the study. Patients received treatment as follows: TMTX 110 mg/m^2 i.v. infusion over 60 minutes on Day 1; FA 200 mg/m^2 i.v. bolus and 5-FU 500 mg/m^2 i.v. bolus on Day 2; followed by 15 mg of FA po q6 hours $\times$ 7 doses. Treatment was repeated weekly for 6 weeks followed by 2 weeks of rest. Patients were treated until disease progression or the presence of unacceptable toxicity.

Results: No grade 3 or 4 neutropenia was seen. Diarrhoea (grade 3/4 NCI) occurred in 38% of patients and allergic reaction (chills) grade 3/4 in 12% of patients. 32 patients are evaluable for response. 13 patients (38%) achieved a partial response. The median duration of response was 10 weeks.

Conclusion: The combination of TMTX, 5-FU + FA is an effective regimen for the treatment of metastatic colorectal cancer. Further studies comparing this combination with standard treatment are currently underway.

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Phase I/II study of CPT-11 in combination with LV2FU5 (De Gramont-Regimen) every 2 weeks for the treatment of colorectal cancer (CRC) after 5FU failure

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The Topoisomerase I inhibitor CPT-11 has demonstrated outstanding activity in 5-FU resistant CRC. LV5FU2 is considered as reference regimen in 1st line CRC in France. This phase I/II study for determination of the maximal tolerated dose (MTD) of CPT-11 and efficacy assessment combines increasing dosages of CPT-11, given on day 1 before the fixed LV5FU2 regimen (days 1, 2) at full dose repeated every 2 weeks. 30 patients have so far been treated· median age 60 (41–69) years, 23 male, 7 female, 15 colon (C), 9 rectum (R), 6 C + R, nb. of previous 5-FU based lines: 2 (1–6).

CPT-11 dose (mg/m^2)	100	120	150	180	200
No. of patients	6	5	6	6	5
No. of cycles	63	47	29	16	5

No dose limiting toxicity has been observed at 1st cycle of all levels. Out of 160 cycles available for toxicity, 25 were delayed and in 3 cycles dose was reduced. 2 febrile neutropenias were reported: 1 at cycle 5 of 1st dose level (100 mg/m^2), 1 at cycle 2 of 3rd dose level (150 mg/m^2). 2 grade 3 delayed diarrhoeas were observed at cycle 1 of 5th dose level (200 mg/m^2). 20 patients are evaluable for efficacy: 1 CR, 4 PR, 2 MR ($\geq$40%), and 1 patient with significant improvement of respiratory symptoms and X-ray (not measurable since lung involvement >50%).

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Effect of chemotherapy with 5-fluorouracil on intestinal permeability of patients with advanced colon cancer

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Background: A common side effect of treatment with 5-Fluorouracil (5-FU) in association with folinic acid (FA) for advanced colon cancer is diarrhea, which can be fatal and is the major obstacle to using high doses of 5-FU.

Purpose: To evaluate whether therapy with FA and 5-FU induces alterations of intestinal permeability in pts with advanced colon cancer and whether these changes correlate with the gastrointestinal symptoms.

Methods: In 16 pts (7 M, 9 F, mean age 60 $\pm$ 12) with advanced colon cancer, small intestinal permeability was assessed by the cellobiose/mannitol (CE/MA) test before and after a 5-day course of chemotherapy with FA (100 mg/sqm i.v.) and 5-FU (450) mg/sqm i.v.). Gastrointestinal symptoms were recorded by the pts for 1 week before chemotherapy until the second CE/MA test was performed.

Results: (mean $\pm$ SD): After chemotherapy, small intestinal permeability increased from 0.016 $\pm$ 0.011 to 0.029 $\pm$ 0.025 ($p < 0.05$) A correlation between the changes in CE/MA values and the number of days with diarrhea ($p = 0.05$) was observed, while no relationship was found with the number of days with stomatitis.

Conclusions: Diarrhea due to chemotherapy with FA and 5-FU ill pts with advanced colon cancer appears to be related to small intestinal damage, as indicated by the increased permeability.

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CPT11 alternating with 5 fluorouracil (5 FU) folinic acid (FA): A multicentre phase II study in 1st line chemotherapy (CT) of metastatic colorectal cancer (CRC): Preliminary results

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Rationale: CPT11 is a topoisomerase I inhibitor with proven activity as single agent metastatic CRC. 5 FU/FA is the mainstay of chemotherapy in