synergistically with mitomycin C (MMC), the following randomized phase II study using a "pick the winner" design was undertaken.

**Methods:** 68 patients with ACC cancer who, had received prior palliative 5-FU/leucovorin-based chemotherapy were randomized to either CPT-11 120 mg/m$^2$ on days 1 + 15 plus MMC 8 mg/m$^2$ on day 1 (arm A) or oxaliplatin 85 mg/m$^2$ on days 1 + 15 plus MMC 8 mg/m$^2$ on day 1 (arm B); in both treatment arms, courses were repeated every 4 weeks.

**Results:** 57 patients are presently evaluable for treatment response and toxicity. The objective response rate in arm A is 7/30 (23.3%; 95% confidence interval [CI], 9.9 to 42.3%) as compared to 5/27 in arm B (18.5%; 95% CI, 6.3 to 38.1%). Median time to progression and overall survival have not been reached yet. The regimens were not equitoxic as indicated by the incidence of severe adverse reactions requiring dose reductions (40% vs. 11%), treatment delays (25 vs. 10 courses), and early discontinuations (27% vs. 11%) in arm A and arm B, respectively. The most common toxicities in arm A were granulocytopenia (83%), thrombocytopenia (47%), diarrhea (53%), emesis (53%) and alopecia (97%). In arm B, common toxicities included granulocytopenia (56%), thrombocytopenia (74%), emesis (59%) and peripheral neuropathy (41%).

**Conclusion:** Both combination regimens seem to be effective in 5-FU/LV pretreated patients with ACC, though the observed response activities do not seem to exceed the single agent activity previously reported for CPT-11 and oxaliplatin alone.

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## Preoperative chemoradiation plus intraoperative presacral electrons in T3–4 Nx M0 primary rectal cancer: Early single institution experience

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**Purpose:** Intense local therapy including intraoperative electron radiotherapy (IOERT) and preoperative chemoradiation has been explored in locally advanced rectal cancer to induce tumor downstaging and promote pelvic disease control.

Materials and Method: From 4/95 to 12/99, 43 T3–4 Nx M0 50 primary rectal cancer patients have been treated with preoperative radiotherapy (45.0 to 50.4 Gy) and simultaneous 5FU (500–1000 mg/m$^2$ days 1–4 and 22–26) or oral Tegafur (1200 mg/day continous daily through 1 to 28 of radiotherapy). Radical surgery was performed 4 to 6 weeks after the completion of induction tratment and IOERT (10 to 15 Gy) was added to the presacral region. Adjuvant chemotherapy using 5FU and Leucovorin (4 to 6 cycles) was recommended.

**Results:** Tolerance to treatment was acceptable. Median age was 65 years (range 36–82). There were 34 males and 16 females. Tumor distance from anal verge was less than 5 cm in 15 (30%). Tumor downstaging pathologic findings were: 10 T1, 19 T2, 21 T3–4, 38 N0 and 12 N+, 22 T mic. Sphincter preservation has been achieved in 32 (64%) patients. Median follow-up time is 17 moths. Pelvic tumor control rate is 97%.

**Conclusions:** Intense local therapy as described is feasible, acceptably tolerated and able to induce significant tumor downstaging effect and encouraging disease control results in primary locally advanced rectal cancer. Up-dated results will be presented.

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## A prospective comparison of in-patient versus outpatient DeGramont therapy: Using quality of life, acceptability and response measures: A pilot study

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**Purpose:** Randomised trial data suggest that the 'DeGramont' regimen (DEG) is now the optimal method of administering 5-Fluorouracil (5FU) and folinic acid (FA) for colorectal cancer. However, the regimen requires hospitalisation for 48 hours, every 2 weeks. As part of a feasibility study for a large UK multicentre trial, we initiated a pilot study to compare cost-evaluation and clinical effectiveness of the inpatient (IP) versus outpatient (OP) DEG.

**Method:** Central line insertion (CLI) for OPs was a day-case procedure by trained nurses. Compliance, costs, response measures and face-to-face quality of life (QOL) were measured in 26 patients given the choice of 12 courses of either IP or OP DEG.

**Results:** 13 patients were enrolled into each arm. Failure of compliance for the first 6 cycles occurred in 54% IPs compared with 8% OPs ($p = 0.001$). After 12 cycles of DEG 92% OP and 50% IP had stable disease ($p = 0.01$). OP costs were estimated at 50% of bed costs. Treatment delays were significantly more common in IPs mainly due to bed shortages. QOL was significantly superior in OPs.

**Conclusion:** Three key requirements to convert IP to OP were identified: CLI, prefilled disposable elastomeric infusors; education of patients and/or carers on changing infusors. Factors determining feasibility of OP DE include availability of CLI, patient and clinical preference. We conclude although OP DEG is practical, cost effective and offers considerable QOL benefits, some patients and hospitals may still need IP delivery.

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## Disease oriented treatment of metastatic colorectal cancer (CRC) with dose-dense 5-FU/Folinic acid (FU/FA) combination chemotherapy

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Treatment of metastatic CRC remains a palliative approach, which should emphasize on quality of life and survival prolongation. Continuous infusion of FU in CRC has been found to be equally effective as FU-Bolus but with significantly reduced hematological and peripheral toxicity. FU as weekly 24-hours continuous infusion up to 2600 mg/m" combined with high-dose FA provides a 3-fold increased dose intensity compared to standard bolus FU/FA protocols, an increased frequency of tumor cell targeting, a favorable toxicity profile and activity in FU/FA pretreated patients. This type of short term and high dose administration of FU was chosen for disease oriented treatment: chemotherapy in case of documented progression (UICC-criteria, including tumor related symptoms), no treatment with stable disease, defined as identical results in two consecutive follow-up procedures. A treatment free progression interval (TFPI) of >5–6 months resulted in administration of the previous protocol, otherwise change to a different combination. Protocols: FU/FA: weekly FA 500 mg/m"/2–4 hrs + FU 2.500 mg/m"/24-hrs; LIF: FU/FA + alpha-Interferon 9 mio I.E. day 1 before FU; MFL: FU/FA + Mitomycin 5–6 mg/m"/24-hrs on day 2. Time schedule: 6 wkly treatments > restaging > continuation for additional 6 wks if no progression of disease > restaging. Patients profile: 115 pts.; median age: 63.4 (37–76); m/w: 74/41; ECOG-Status: 0: 38, 1: 67, 2: 10. Immediate response to treatment (after 12 wkly treatments): CR: 12.6%, PR: 32.2%, NC: 39.1%, PD: 11.5, ND (disease not measurable): 4.6%; response after one TFPI: CR: 4.6%, PR: 13.6%, NC: 43.7%, PD: 29.9%, ND: 8.0%. Median duration of TFPI: 5.0 months (range: 3–27). Median survival in months: all pts: 23.4; no TFPI: 11.0; 1 to n TFPI,s of >3 months: 31.0. Toxicities: no grade III/IV hematologic toxicity, 6/115 with grade III diarrhea, 22/115 with a reversible hand-foot-syndrom and LIF.

**Conclusions:** disease oriented chemotherapy improves the prognosis for the majority of pts. with metastatic CRC. This strategy focuses for the first time on the patient,s individual tumor biology. Short duration, high dose intensity and frequency of FU administration seems to be essential. Implementation of new drugs (CPT-11, Oxaliplatin) will have additional benefit.

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## Prevention and treatment of carcinomatosis from colorectal malignancy

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**Background:** At the time of surgical exploration of the abdomen, approximately 10% of colon cancer patients will be found to have peritoneal seeding. Also, approximately 30% of patients will have disease recurrence within the resection site or on peritoneal surfaces. Phase II studies of peritonectomy procedures and intraperitoneal chemotherapy using mitomycin-C and 5-fluorouracil were employed in an attempt to change the outcome of this clinical situation from a terminal event to long-term survival.

**Methods:** Patients with primary or recurrent colorectal cancer with peritoneal seeding were evaluated using the Peritoneal Cancer Index (PCI). This is a quantitative prognostic indicator that uses nodule size and distribution to arrive at a numerical score. Also, a Completeness of Cytoreduction Score (CC) based on the extent of cancer following an aggressive cytoreduction was utilized. Other parameters were statistically evaluated.

**Results:** The PCI was shown to be a prognostic indicator capable of accurately predicting the results of these aggressive treatments ($p < 0.0001$). Also, the CC score had predictive value ($p < 0.0001$). Patients who had carcinomatosis treated in conjunction with a resection of their primary colon cancer showed statistically improved survival over those treated m the setting of recurrent colorectal cancer ($p = 0.02$).