a large number of SNP's based on analysis of individual samples is time consuming and expensive.

**Materials and methods:** We have established a pooling strategy for detection of SNP's in genes, which are known in the pathogenesis of colorectal cancer, including APC, beta-catenin, E-cadherin, K-ras, p53 and others. The SNP's are selected from the dbSNP-NCBI database (). We have constructed pools of DNA from 230 patients with diagnosed sporadic colorectal cancer and from 540 controls. 100 ng. of genomic DNA from each individual is used for the pool. The pool holds DNA for approximately 1500-2000 individual SNP analysis.

The method involves PCR amplification of genomic DNA fragment including the SNP, single base extension (SBE) reaction of SNP using fluorescent-labelled ddNTP followed by capillary electrophoresis of single base reaction products.

We aim at screening 500 SNP's for association with disease development covering approximately 50 genes.

**Results:** SNP's are screened by analyzing frequency in case-pool and in control-pool. SNP's showing a minor allele frequency of >10% are further analyzed, and candidates showing difference in allele frequency between the two pools are further validated by sequencing.

**Preliminary results screening 63 SNP's in 7 genes show:**

Positive PCR product Positive SBE product Minor allel frequency >10% Non conclusive data

60/63 = 95% 59/61 = 97% 25/61 = 41% 2/61 = 3%

The total number of single reactions for screening of the 63 SNP's in pools is 704 as compared to 48.510 reactions by analyzing individual samples, thereby reducing the number of analysis by a factor of 69.

**Conclusions:** We have established a method for screening of large number of SNP's in genes suspected for a potential role in development of sporadic colorectal cancer. The method significantly reduces the total number of reactions and the amount of DNA used for SNP analysis, as compared to analysis of individual samples, and identifies SNP's suspected for association with disease development.

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## Effects of capecitabine (Xeloda) on quality of life (QoL) in patients with metastatic colorectal cancer (MCRC)

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**Background:** While outcomes such as objective response, time to disease progression and overall survival are well-established measures of treatment response, the QoL benefits of oral treatments, such as the novel fluoropyrimidine capecitabine (Xeloda®), are important when choosing appropriate therapy for MCRC.

**Patients and Methods:** QoL was assessed in a sample of 209 patients receiving oral capecitabine as second- or third-line therapy for MCRC. Patients completed the EORTC QLQ C-30 questionnaire and the specific model for colorectal cancer (CR-38) at baseline, before the first cycle of treatment, at weeks 7 and 13, and at the end of treatment. Linear models with repeated measures of the scores were used to analyse questionnaire responses over time. The proportion of patients with an improvement, stabilisation or worsening of QoL scores from week 7 onwards was analysed with generalised linear models for repeated measures, using the generalised estimating questions technique. Statistical analysis was performed using an SAS programme (system version 8.2).

**Results:** Patient characteristics were as follows: male/female, 54.5%/45.5%; mean age 53.9 years (range 25.0-72.0 years); white/Caucasian, 89%. Almost 50% of patients completed the questionnaires at all time points. Variables for which a statistically significant improvement in QoL over time was detected included global health status (p=0.04), physical functioning (p=0.04), financial problems (p=0.008), future perspective (p=0.006) and weight loss (p=0.0008). The proportion of patients that remained stable or improved was * 70% for most scales. At least 30% of patients reported improvements in the following QoL scales from week 7 onwards: global health status (38%); social functioning (36%); fatigue (36%); pain (35%); micturition problems (33%); role functioning (31%); emotional functioning (31%); future perspective (31%); chemotherapy side-effects (31%). After all time points *"at the end of treatment?"*, 46% of patients showed an improvement in global health status and 24% had stable scores. In addition, 45% of the total number of patients experienced improvement in fatigue and 43% had improvement in social functioning.

**Conclusion:** These findings indicate that the efficacy, safety and convenience of capecitabine allow patients to maintain a normal lifestyle and have a direct impact on QoL. This important measure should be considered along with established treatment outcomes when deciding on patient therapy in MCRC.

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## Peritoneal carcinomatosis of colorectal origin: results of palliative surgery and systemic chemotherapy.

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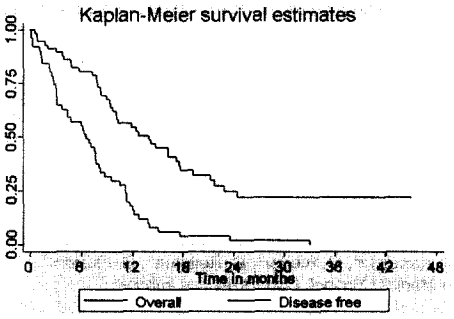
**Back ground:** Peritoneal carcinomatosis (PC) has a grave prognosis. New treatments like extensive surgical resection and intra-peritoneal chemotherapy may enhance survival. This novel treatment seems to create an improved survival in patients with PC of CRC origin without distant metastasis. Very little is known about the results of systemic chemotherapy in these patients.

**Methods:** 57 patients with proven peritoneal carcinomatosis of colorectal origin without distant metastasis treated with palliative surgery and fluorouracil (5FU)(400mg/m$^2$) and folinic acid (80mg/m$^2$) once weekly, or irinotecan (CPT 11) (350mg/m$^2$) every three weeks in patients treated with 5FU within 12 months prior to study entry were studied. The median follow-up was 40 months (range 2.5 - 62 months). The following prognostic factors were analysed: gender, location of primary CRC, PC at diagnosis CRC or recurrent CRC and palliative resections. Analysis: Survival and progression free survival was calculated by the Kaplan Meyer method. Prognostic factors where analysed using the log-rank test.

**Results:** The median survival of peritoneal carcinomatosis was 14.1 months when treated by palliative surgery and systemic chemotherapy. Median progression free survival was 7.7 months. Kaplan Meyer curves are shown in the figure Female gender correlate with improved survival, but this did not reach significance (p=0.0741). Patients in whom a resection was possible had a significant better prognosis (improvement from 8.3 to 17.3 months (p=0.0042)). None of the other factors were related to survival.




**Conclusion:** Survival of PC of CRC origin is poor when treated by palliative surgery and systemic chemotherapy only. If a palliative resection is possible the survival significantly improves probably related.

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## Equal prognosis of elderly and non-elderly patients with metastatic colorectal cancer and 5-FU treatment: a retrospective analysis.

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**Introduction:** There is, uncertainty as to what extent systemic adjuvant or palliative chemotherapy should be offered to elderly patients with colorectal cancer. This fact is related to the unfortunate underrepresentation or even