ical study revealed ^{ac}pT3 lower rectal cancer. The external irradiation was performed with a 10MVX delivering 30–40 Gy/15–20 Fr to the entire pelvic cavity. RALS was performed 30–40 Gy/3–4 Fr (dose evaluation point set at 1.0 or 1.5 cm from the source). After a mean waiting period of 14 days after irradiation, abdomino-perineal resection (APR) was performed in 34 cases and low anterior resection (LAR) in four. In the N-RT group, the surgical procedure was APR in 13 cases and LAR in six.

Results: Five and 8-year survival rates were 83 and 83% in the RT group, and were 80 and 80% in the N-RT group. The local recurrence rate was 5% in the RT group in contrast to 21% in the N-RT group.

Conclusion: Although a significant enhancement of the survival rate was not achieved by preoperative radiotherapy with external plus intraluminal irradiation for advanced lower rectal cancer, this treatment contributed to excellent local control and a decrease in the local recurrence rate.

260 PUBLICATION

A phase II study of alternating cycles of CPT-11 and high-dose 48 hour infusion 5-FU in combination with leucovorin (HD-5-FU/LV) in no selective patients with metastatic colorectal cancer (MCRC)

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Purpose: A weekly 48 hour infusion of HD-5-FU/LV and CPT-11 are effective in the treatment of the MCRC. Even if CPT-11 seems to have incomplete cross-resistance with 5-FU, pharmacodynamics data recommend caution in evaluating their combination. For this reason we performed a trial in which CPT-11 and HD5-FU/LV were administered on alternating cycles.

Methods: No selective 20 pts with MCRC received 5-FU 2600 mg/m^2 over 48 hrs q wk × 4 in combination with LV 150 mg/m^2 followed by a 2-week rest, and then CPT-11 350 mg/m^2 q 3 wks. Median age = 68 (45–79); PS (WHO): 0/1/2, 3/15/2. Most frequent metastatic sites were liver 12 (60%) and lung 6 (30%). 5/20 pts were pretreated for metastatic disease and "bulky" disease was diagnosed in 8 cases before treatment.

Results: All patients were evaluable for toxicity and 18 for response. 2 pts achieved, a CR and 2 pts achieved a PR for an overall response rate of 22%. 12 pts (66%) reported a stable disease. An assessment of median time to tumor progression and survival are in progress. The incidence of grade 3–4 toxicity for patient in any cycle is for CPT-11: diarrhea 10%, naus/vom 10%, neutropenia 15%; for HD-5FU/LV: diarrhea 5%, naus/vom 5%, stomatitis 15%.

Conclusion: An alternating regimen of CPT-11 and HD-5-FU/LV is active even if the preliminary response rate is not clearly different than that of either CPT-11 or HD-5-FU/LV alone. Therefore, the high percentage of stable disease, the unfavourable characteristics of pts and the low toxicities stimulate us to continue our study.

261 PUBLICATION

Phase-II-study of a 24-h infusion with 5-fluorouracil (5-FU) and simultaneous sodium-folinic acid in the first-line-treatment of advanced colorectal cancer: Interim analysis

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Introduction: Weekly continuous high dose therapy with 5-FU and Calcium-folinic acid (Ca-FA) according to "Ardalan" has shown to be an effective treatment in advanced metastatic colorectal cancer. Sodium-folinic acid (S-FA) is a new formulation, which in contrast to Ca-FA allows the simultaneous iv-administration in one pump. Thus, the effect of both drugs might be augmented due to improved 24 h-kinetics. Purpose of this study was to evaluate effect and toxicity of this new combination.

Methods: Since 1997 50 patients with metastatic colorectal cancer have been recruited to receive weekly 24 h-infusions of 5-FU (2600 mg/m^2) and S-FA (500 mg/m^2) combined in one pump for 6 weeks. Treatment was repeated after a 2-week rest period.

Results: 28 patients having either received at least 2 courses of chemotherapy or showing early progression up to now are evaluable for response according to study protocol. Their median follow up is 8 months. Of these the response rate for CR and PR was 50% (14/28) with 1 CR (3.6%), 13 PR (46.4%), 11 NC (39.3%) and 3 PD (10.7%). The worst toxicities experienced by 43 evaluated patients (106 treatment courses) were gastrointestinal side effects. Grade IV diarrhea appeared in 3.8%, grade IV stomatitis in 0.9% of the treatment courses. Grade III hand-foot-syndrom was seen in 3.8%, grade III diarrhea in 7.5% und grade III stomatitis in 2.8%. Treatment was stopped in one patient due to cardiac toxicity after the third administration in the first course.

Conclusion: The early data in this study indicate a potentially augmented effectiveness for weekly simultaneous 24 h-infusion therapy with 5-FU and S-FA in metastatic colorectal cancer. Treatment is feasible with respect to toxicity.

262 PUBLICATION

The distribution of polymorphic enzymes in colon cancer case

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Purpose: The polymorphic enzymes N-acetyltransferase (NAT2), glutathiontransferase M1 (GSTM1), and T1 (GSTT1) are predisposing factors for several human cancers. Colon cancer is associated with genetic, occupational, and enviromental factors. Therefore, several studies for genotyping this enzymes were performed on colorectal cancer cases. Most of these studies revealed an overrepresentation of the rapid acetylator status.

Methods: The distribution of NAT2, GSTM1, and GSTT1 was investigated in 80 colon cancer cases and 140 controls (suffering from non-malignant diseases) in a case-control study. They were genotyped from leucocyte DNA by PCR and RFLP. Additionally, possible occupational and non-occupational exposures to carcinogens were investigated using a questionnaire.

Results: In the cancer cases 65% were "slow" acetylators, 53% were GSTM1 negative and 15% were GSTT1 negative. In controls 61% were "slow" acetylators, 51% were GSTM1 negative and 14% were GSTT1 negative. The results presented are in line with the assumption, that the enzym status of the polymorphic enzymes NAT2, GSTM1 and GSTT1 cannot be seen as a general genetically determined risk factor for colon cancer.

Conclusion: The impact of occupational and/or environmental factors in an industrialized area with a known elevated colon cancer mortality might be considered as possible cause for the ordinary distribution of the "slow" NAT2 genotype in the cases investigated.

263 PUBLICATION

Oxaliplatin (OX) after irinotecan (IRI): Antitumour activity and clinical benefit of 3rd and higher line chemotherapy with ox for patients (pts) with metastatic colorectal cancer (MCC) after failure of IRI

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Purpose: There is no data concerning the use of chemotherapy (CT) alter failure of IRI, an agent that is active in 2nd-line CT for MCC.

Methods: All pts in eight german centers who received an OX-containing regimen after they had been treated with IRI (350 mg/sqm q3w) as 2nd -or higher-line and progressive disease (PD) occurred were analysed for best response (BR) to IRI to OX and for subjective response rate (SRR) or clinical benefit in pts with tumour related symptoms (TRS).

Results: Out of 34 identified pts all but 4 showed PD while receiving IRI or within 6 weeks after last IRI. In 17 pts PD was BR to IRI defined as primary resistance (IRIPRIRE). 11 pts were treated with single agent OX (130 mg/sqm q3w) while in 23 cases different combination regimens with OX and folinic acid and high dose infusional 5-Fluorouracil (OX-HDFAFU) in full dose was administered. OX was 3rd-line in 23 pts and higher line in 11 pts.

Efficacy: PR. 4 pts (ITT 12%), MR or NC: 15 pts (tumour control rate 56%), PD: 3 pts, not evaluable 3 pts. TTP from start of OX was 1 to 17 months (m), median 3 m. 18 pts suffered from TRS that improved in 8 while receiving OX (SRR 44%). ORR and SRR were poorer in pts treated with single agent Ox. IRIPRIRE: Out of 17 pts 3 achieved a PR and 8 NC (median TTP and SRR comparable to whole group).

Conclusion: Our analysis indicate that OX-HDFAFU might be considered in pts with MCC progressing under IRI and underline the lack of cross resistance of the two regimens in a clinical setting.