

was lost to follow-up. There have been 4 deaths from disseminated disease, and 4 patients admitted in the first 6 weeks after treatment for various reasons. No patient experienced liver failure or veno-occlusive disease. Responses measured by CEA and CT or MRI scans showed that 25% of patients had at least a >50% reduction in tumor burden; 55% of patients had stable disease or <50% response, and 20% of the patients failed distantly.

Conclusion: Radioactive 90-yttrium microspheres induce a 25% partial response rate in patients with chemo refractory metastases from colorectal cancer. It is a safe and low toxicity outpatient treatment in the dose range reported.

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POSTER

Sphincter preserving procedures for low rectal cancer

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Introduction: Total rectal resection (TRR) with coloendoanal anastomosis (CEAA), mesorectum 'en bloc' excision (TME), radical abdomino-pelvic lymphadenectomy (RAPL) and J colic reservoir represents a valid alternative to the traditional surgery for the restorative management of low rectal cancer.

Methods: We report our experience at National Cancer Institute of Milan, Italy with this procedure. From March 1990 to December 2000, 346 consecutive TRR with CEAA were performed at our Institute; 262 patients, with a minimum follow-up of 18 months, were treated for a primary cancer of distal rectum at a distance ranging from 3 to 8 cm within the anal verge. Patient's stratification based on definitive pathological report staging was 64 (20%) Dukes' stage A, 101 (32%) stage B and 155 (48%) stage C.

Results: Overall recurrence rate was 8.7%; (23 patients) pattern of local recurrence according to stage of disease was 3 Dukes' A, 6 Dukes' B and 14 Dukes' C after an interval ranging from 8 and 47 months. A specific pathologic evaluation was performed by a dedicated pathologist (S.A.) in the last consecutive 147 cases.

Blood vessel invasion (BVI) was present in 10 out of 51 No patients. Tumour recurrence occurred in 5 out of 41 BVI+ patients versus 3 out of 41 BVI- patients (2 positive distal resection margin and one positive circumferential margin of mesorectum). Perineural invasion (PNI) was present in 8.8% of 45 Dukes B patients and 41.1% of 73 Dukes C patients (47% N1 and 53% N2). In the 17 PNI+ patients local recurrence occurred in 74% (35% N1 and 65% N2) versus 45% of 15 PNI- patients (40% N1 and 60% N2). Four Dukes A patients and 17 Dukes B patients have distal resection margin (DRM) less than 9 mm (median follow-up 40 months). No recurrence occurred in Stage A patients; 3 Stage B patients had lung metastases (2 BVI+ and one DRM+), one experienced local recurrence (DRM+). Dukes B patients received postoperative radiotherapy.

Conclusion: Our data, in accordance with other authors, seem to highlight that important pathologic prognostic factors turned out to be BVI in No patients, PNI in C patients. DRM less 9 mm plus RT did not influence clinical outcome of No patients.

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POSTER

Thymidylate synthase and p53 expression do not predict chemotherapy outcome in metastatic colorectal carcinoma

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Introduction: Thymidylate synthase (TS) and p53 have been reported to predict the results from chemotherapy in advanced colorectal carcinoma (ARCR).

Methods: One hundred and twenty-two patients with ARCR have been treated with 5-fluorouracil (5-FU)-based therapy at the University Hospital in Uppsala in four different randomised clinical phase III studies between 1989 - 1997. The paraffin-embedded tumours at primary diagnosis were retrospectively analysed with immunohistochemical technique. TS enzyme levels were evaluated using the monoclonal antibody TS 106 and the p53 expression with the monoclonal antibody DO-7.

Results: Fifty-three (43%) of the patients had advanced disease at diagnosis. There were 26% radiological responders. Seventy-eight % had high TS expression and 60% of the tumours were p53 positive. None of the markers predicted the outcome of the later palliative treatment. However, the TS values had prognostic information and significantly predicted time

to recurrence (median for low TS 30 months and for high TS values 11 months, $p = 0.001$).

Conclusion: Immunohistochemical investigation of TS and p53 of the primary cancer is not useful to predict outcome after palliative chemotherapy in ARCR. TS can instead be regarded as a marker of proliferation.

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POSTER

Expression of CEACAM6 in colorectal cancer: significant association with overall and disease-free survival

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Members of the carcinoembryonic antigen family, CEACAM1, CEA, and CEACAM6 are co-expressed in normal colorectal epithelia but are deregulated in many colorectal tumors. Very recent studies have shown that human CEACAM1 which is often downregulated in colorectal cancers has tumor suppressive activity in prostate cancer. CEA or CEACAM6 which can block differentiation, disrupt cell polarization and tissue architecture, and inhibit apoptosis (anoikis) are overexpressed in many human tumors. The aim of our study was to investigate a possible relationship between tissue expression of these functionally active molecules and prognosis in patients with colorectal cancer. Patients have been enrolled in a randomized, controlled clinical SAKK study. Immunohistochemical analysis was carried out on tissue microarrays from 240 paraffin embedded biopsies with specific monoclonal antibodies (mabs) against CEACAM1, CEA, or CEACAM6. Staining of tumor microarrays was scored from negative (-) to strongly positive (+++). Long-term overall (OAS) or disease-free survival (DFS) in patients with enhanced (++/+++) or reduced (-/-) individual CEA family antigen expression was calculated by use of Kaplan-Meier estimates and the Cox proportional hazards model. The median follow up time was 13 years. Tissue expression of CEACAM1 was reduced (-/-) in 102 patients whereas CEA and CEACAM6 were enhanced (++/+++) in 226 and 132 patients, respectively. CEACAM1 or CEA showed no significant relationship to overall or disease-free survival of colorectal cancer patients. In the case of CEA, however, only 14 patients showed reduced expression. In contrast, univariate analysis demonstrated that enhanced expression of CEACAM6 (55.4%) was associated with far worse OAS (hazard ratio = HR, 2.19; $p = 0.00014$) and DFS (HR, 2.44; $p = 0.000029$). Multivariate Cox analysis including sex, age, tumor localization, tumor staging, lymph node status, and treatment showed that CEACAM6 overexpression independently predicted survival (OAS, HR, 1.89; $p = 0.0027$; DFS, HR, 2.00; $p = 0.0085$). To our knowledge this study is the first to demonstrate the prognostic significance of immunohistologically detectable overexpression of CEACAM6 in patients with resectable colorectal cancer. This may help to identify patients who need to be selected for adjuvant treatments or an intensive postoperative follow-up protocol. The data are in good agreement with recent functional findings.

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POSTER

Extended phase I study of capecitabine and weekly irinotecan as first-line chemotherapy in metastatic colorectal cancer

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Purpose: Capecitabine (CAP) demonstrated efficacy in metastatic colorectal cancer (CRC). Preclinical data on nude mice bearing human colon tumor xenografts demonstrated significant synergistic antitumor activity for the