−93% and −25% respectively) with XELODA (TM). XELODA (TM)-patients received more days of treatment (usually topical preparations) for HFS. Use of colony stimulating factors was infrequent in both arms. Physician consultations and other medical procedures for treatment of these AEs did not involve a significant amount of medical resource use.

Conclusion: Oral administration of XELODA (TM) avoided 336 overnight stays and 5,756 outpatient visits for IV administration of drug. XELODA (TM) treated patients needed 184 fewer hospital days for the treatment of related AEs and less use of high-cost medications for AEs. Despite higher drug acquisition costs for XELODA (TM), overall cost savings are likely if it is used instead of the Mayo regimen.

208 POSTER DISCUSSION

Functional results after total mesorectal excision (TME) in rectal cancer

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Introduction: The primary objective of total mesorectal excision (TME) in the surgical management of rectal cancer is to achieve local tumour control. An important aspect of this technique is preservation of the autonomic nerves and the related sexual and bladder functions, if oncologically feasible. Since a low anastomosis is performed after TME in most patients, preservation of a more or less normal defecation is also important for quality of life.

Methods: A total of 88 patients with rectal cancer were managed by TME and preservation of the autonomic nerves between 1996 and 1999. Functions of defecation, voiding and sexual function were assessed preoperatively and postoperatively during follow-up with a scoring system.

Results: After a mean follow-up period of 13 months erectile or ejaculatory dysfunction in 33% of male patients was observed. Patients who had received preoperative radiotherapy (5 × 5 Gy) had better scores for postoperative sexual function than those who did not receive radiotherapy. Voiding was disturbed in 18% of patients and did not improve significantly with a longer follow-up. In patients with a low anastomosis, 41% experienced a social handicap because of frequency of defecation or soiling.

Conclusion: Quality of life after TME will be determined for a large part by postoperative functional results. In this study a clear relation between the length of follow-up and degree of sexual and bladder dysfunction was not found.

209 POSTER DISCUSSION

Late side effects of combined treatment modalities in rectal cancer

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Purpose: Combined treatment modalities are increasingly used for the treatment of rectal cancer. The combination of radio- and chemotherapy is known to increase the severity of acute side effects. The data on the frequency and origin of late sequelae, however, is conflicting. The goal of this analysis was to determine the frequency and extent of late side effects and to define prognostic factors for their occurrence.

Methods: The data of 53 patients with rectal carcinoma (primary tumors n = 33, recurrent tumors n = 20) were evaluated retrospectively with regard to late side effects. The patients received radiotherapy (RT) only (n = 19) or a combined radiochemotherapy with 5-FU (n = 34). 41 patients also underwent surgery prior to irradiation or after it. The follow-up was 580 ± 359 days with a median of 493 days.

Results: Radiation enteropathy was found to be the most frequent late sequela (35/53 cases). It was mild in 23 cases (43.4%, EORTC/RTOG grade 1 and 2), whilst 12 patients (22.6%) suffered from severe enteritis (grade 3, 4 and 5). 8 patients (15.1%) required reoperations for late bowel complications. Median time of complication occurrence was 6.8 months after the initiation of RT. Significant risk factors for late bowel complications turned out to be simultaneous chemotherapy (p = 0.03) and surgical treatment as part of the combined treatment plan (p = 0.03).

Conclusion: Our results indicate that the combination of radio- and chemotherapy in the treatment of rectal cancer increases the frequency of chronic intestinal side effects. These can cause considerable morbidity and reduce the patients' quality of life. Irradiation techniques and supportive care have to be improved to prevent severe late effects.

210 POSTER DISCUSSION

Liver resection after preop. chemotherapy for colorectal metastases: Morbidity and treatment results

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Problem: In patients with colorectal liver metastases not amenable to surgical resection or presenting with poor risk factors, preoperative treatment may be advisable. We analysed the impact of preop. therapy upon subsequent resection in terms of morbidity, mortality, and survival.

Patients and treatment: From 1993–98, 127 liver resections were performed. Of these, 37 resections (29%) followed systemic or regional chemothp. Median patient age: 61 (35–71 yr). Chemothp: 5-FU/LV (Mayo scheme), HD 5-FU (2.6 g/msq)/LV, or 5-FU/LV/oxaliplatinum. Time interval between start of chemotherapy and liver resection was 12 mos. in median (2–16 mo.)

Results: Resectional procedures: hemihepatectomy (S4/5-8, n = 10), segmental resections (n = 19), plurisegmentectomies (n = 8); mortality: 2.7%. Morbidity: 28 pat. (76%) with uneventful course.; complications: pneumonia (n = 2), bile leakage, (n = 2), bleeding (n = 2), jaundice (n = 2), SIRS/ARDS (n = 1). Radical resection (R0) was possible in 29 patients whil another 8 pat. showed extrahepatic spread at laparotomy. Median survival is 25 mos. (4–38+ mos.)

Conclusion: Resection of residual liver lesions after systemic or regional chemotherapy can be performed with very limited morbidity and mortality This approach may offer cure even for patients not amenable to resection as the treatment of first choice.

211 POSTER DISCUSSION

Artificial neural network prediction of 5-year survival from colon cancer

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Purpose: To determine the effectiveness of computer-based artificial neural networks (ANNs) in predicting 5-year survival from colon cancer.

Methods: 400,000 cases from the National Cancer Database with 79 variables for each patient were used in the analysis. Advanced computer technology was used to identify the most important variables for predicting 5-years survival. Thirteen variables were identified in this manner and were used as inputs to an advanced artificial neural network. Evaluation of accuracy was based on the ANNs performance on an additional 1000 patients ("validation patients‰) that were not used in the design of the neural network solution.

Results: The area under the Receiver Operator Characteristics (ROC) Curve was 82% for the "validation patients.‰ Choosing a point on the ROC Curve that represented optimized overall accuracy resulted in the following: Sensitivity = 67%, Specificity = 82%, 5-year predictive value = 71%, 5-year death predictive value = 79%, Overall accuracy = 76%.

Conclusion: Artificial neural networks were able to predict with clinically useful accuracy, the 5-year survival of colon cancer patients. In addition, the program generalized very well to patients that were not used in the development of the solution.

212 POSTER DISCUSSION

Postoperative radiation (RT) and concomitant bolus fluorouracil (FU) with or without additional chemotherapy (CT) as adjuvant treatment in patients with high risk rectal cancer. A randomized phase III study conducted by the Hellenic Cooperative Oncology Group

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Purpose: To compare the impact of postoperative RT with or without additional CT on disease-free survival (DFS) and overall survival (OS) of patients with stage II or III rectal cancer.

Methods: From October 1989 until February 1997, 220 patients were randomized postoperatively to receive either one cycle of CT with FU and leucovorin (LV) followed by pelvic RT with concomitant FU (400 mg/m^2) as

a rapid i.v. injection during the first 3 and last 3 days of RT and three more cycles of the same CT with FU and LV (group A, 111 patients) or pelvic RT with concomitant FU alone (group B, 109 patients).

Results: As of August 1998, after a median follow-up of 4.9 years, there was no significant difference in either 3-year DFS (group A, 70.3%; group B, 68.2%, p = 0.53) or OS (group A, 77%; group B, 73.3%, p = 0.75). The incidence of severe side effects was significantly higher in patients of group A than of those of group B (32.4% vs 4.6%, p < 0.0001).

Conclusion: The incorporation of additional CT with FU and LV to postoperative concomitant RT and bolus infusion of FU does not offer a 3-year survival benefit over concomitant RT and bolus infusion of FU and increases significantly toxicity in patients with stage II or III rectal cancer.

213 POSTER DISCUSSION

A randomized phase II trial assessing Irinotecan (IRI) and 5FU/folinic acid (LV), "Mayo regimen", in first line palliative chemotherapy patients (pts) with metastatic colorectal cancer (MCRC)

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Single agent IRI is active in MCRC with significant survival advantage over BSC or best 5FU schedule in pts with prior 5FU failure (The Lancet, 31 Oct. 1998). In this randomized phase II, pts were assigned to either (A) IRI at 350 mg/m^2 day (d) 1 q 3 w or (B) LV 20 mg/m^2 I.V. bolus/day (d) + 5FU 425 mg/m^2 as IV bolus/d, d1–d5, repeated every 4 weeks (wks). 159 pts (82 in A and 77 in B) were randomized; 136 pts are treated, eligible and evaluable (65 in A, 71 in B). Tumor assessments were done q 3 cycles (cy) for A arm and q 2 cy for B. After progression pts were crossed-over provided PS ≤ 2 with good renal, liver and hematological functions. Response were reviewed by independent experts (ERRC). The main pts characteristics are comparable between groups A and B: median age 62 vs 58, primary colon/rectum (%) 64/36 vs 57/43, PS 0 53% vs 62% (p = 0.24), number of organs ≥2 44% vs 46%, respectively. A high proportion of pts had synchronous metastasis: 68% in A, 61 in B. Results before cross-over are: 1. Response rate per ERRC in A: 15.4% [95% CI: 7.6–26.5] and in B: 9.9% [95% CI: 4.1–19.3]. 2. TTP in A:6.4 months (m) [range: 0.7–11.6+], B: 3.9 m[range: 1.2–9.8] (p = 0.03) 3. Duration of response and stabilization: A: 7.0 m [range:1.3–11.5+], B: 5.6 m[range:1.4–9.8] (p = 0.015). Results after cross-over and survival will be presented at the meeting. The main NCI grade 3/4 adverse were as expected: neutropenia 41% vs 42%, diarrhea 25% vs 9%, vomiting 9% vs 7% in A and B respectively.

Conclusion: This randomized trial suggests that IRI, single agent, is at least as active as Lv/5FU "Mayo regimen" in first line MCRC pts.

214 POSTER

A pilot study of a feasibility and economic analysis of home based chemotherapy in advanced colorectal cancer

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In the UK, there has been a shift in care towards home or community based treatment following recent changes in Government healthcare policy. This is a pilot study of home chemotherapy for patients with advanced colorectal cancer. The aims are to: 1) quantify the costs of homebased chemotherapy; 2) measure the patient and carer acceptability of this; 3) establish a local home chemotherapy treatment/liaison service.

Method: one senior oncology research nurse was responsible for the treatment and assessment of the patient, with backup from medical staff as required. Eligible patients receiving intravenous regimens of Lokich 5FU (continous), DeGramont 5FU and Folinic Acid (48 hour) and Tomudex(c) were invited onto study to receive home management for the first 12 weeks of treatment. Patients and their caters were administered acceptability questionnaires before treatment, midway and after treatment was completed – their enthusiasm, worry, coping/supporting ability, with regard to home treatment, were scored on an ordinal scale. The costs of travel/phone, nurse time and central venous line costs for DeGramont patients were recorded, to compare against hospital based treatment.

Results: early analysis suggests that enthusiasm was high; patients have low or decreasing worry; patients coped well and carers gave good support.

In analysing the costs of 22 patients entered onto study, an average cost per week per regimen was calculated, and compared with an average cost per week of hospital based care, as shown below:

Hospital: DeGramont-£230.00; Lokich-£92.00; Tomudex-£35.39 Vs. Home £143.67; £46.95; £40.85

We conclude that home managed chemotherapy is acceptable, cost effective and preferred by patients. Following this pilot study, further study on a national scale is being instigated to look at the value of home based chemotherapy.

(Tomudex(c) is a product of Zeneca Pharmaceuticals)

215 POSTER

Thymidylate synthase (TS) protein expression in advanced colon cancer: Correlation with the site of metastasis and the clinical response to leucovorin-modulated bolus 5-fluorouracil (5FU)

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Purpose: Aims of the present study is to test whether the correlation between TS expression and the clinical response is still valid for a bolus 5FU regimen, and to compare TS levels between liver metastases and abdominal recurrences from colon cancer.

Methods: 41 patients (M/F 25/16, median age 60 years) with unresectable metastatic or recurrent colon cancer, treated homogeneously with bolus 5FU and leucovorin

Results: 27 patients (66%) showed high levels of TS expression as defined by a TS score equal to 3 and 4. The proportion of cases with high levels of TS expression was significantly higher in abdominal recurrences (18 of 22, 82%) compared to liver metastases (9 out of 19, 47%; $p = 0.02$). Intratumoral TS protein expression was inversely correlated with response to chemotherapy (response rate: 7/14, 50%, versus 0/27, in patients with low and high levels of TS expression, respectively; $p = 0.0001$).

Conclusions: These results confirm that the level of TS protein expression predicts for response to 5FU, even with a bolus schedule. The higher TS levels observed in abdominal compared to liver metastases may account for their different responsiveness to 5FU chemotherapy.

216 POSTER

Prospective study of adjuvant therapy with monoclonal antibody 17-1A of Dukes' B2/B3-colon carcinoma – Interim analysis of toxicity

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Purpose: Adjuvant immune therapy with the murine monoclonal antibody (mAb) 17-1A has been shown to be an alternative to chemotherapy in the treatment of stage In colorectal cancer presenting similar efficacy in combination with lower toxicity. Therefore we suggested that also patients with Dukes' B colon cancer could have benefit from adjuvant treatment with mAb 17-1A.

Patients and Methods: In 1997 we started this prospective multicentre trial including patients after curative (RO) resection of Dukes' stage B2/B3 adenocarcinoma of the colon. Patients are randomly assigned to either treatment with mAb 17-1A (arm A) or observation regimen (arm B). In the treatment arm patients are administered 500 mg of mAb 17-1A intravenously followed by four infusions of 100 mg every four weeks. So far, 214 patients (114 arm A/100 arm B) have been entered into the trial.

Results: Our interim data concerning toxicity reveal that of 267 courses of mAb 17-1A eligible we saw a total number of 58 (22%) adverse events. Except one case of severe toxicity (exacerbation of Wegener's granulomatosis) all side effects are of WHO grades 1–2 (17% grade 1, 5% grade 2). Adverse events are most frequent within the first course with 39% events (versus 22% in course 2, 17% in course 3, 20% in course 4, 2% in course 5). Diarrhoea, nausea and vomiting represented the most common side effects.

Conclusions: These data underline the favourable toxicity profile of adjuvant treatment with mAb 17-1A, which migt confirm its role in the therapy of the a priori good risk group of patients with Dukes B colon carcinoma.