(16%) and 49 partial response (54%), including 21 (43%) with microscopical residual disease. In 24 patients (27%), stable disease was achieved. No pts progressed locally. There was 1 postoperative death (1.1%). The overall survival in 12 months is 93.5%. With a median follow up of 15 months, 72 patients with radical surgery still alive and disease-free (84.7%), 8 are alive with disease (9.4%) and 5 have died (5.8%): 1 from PD, 2 from treatment complications (1 surgery, 1 postoperative ChT) and 2 from other causes. 9 recurrences were detected: 8 systemic and 1 local plus systemic.

Conclusions: Preoperative treatment with CI of 5-FU and RDT in locally advanced RC was well tolerated, with a remarkable response rate and anal sphincter sparing. Our pathological complete responses are lower than other authors. This may be due to more stage III pts, or the performance of an exhaustive pathological finding of residual microscopic disease after surgery. Results are too preliminary to ascertain if this approach will impact on survival.

1081 POSTER

Multicenter phase II study of irinotecan as second line chemotherapy in metastatic colorectal cancer after prior exposure to infusional 5-FU based chemotherapy

P. Schöffski, U. Vanhoefer, H. Kirchner, G. Trenn, C. Bokemeyer, P. Preusser, W. Achterrath, B. Deuß, H.-J. Wilke. *Med. Hochschule Hannover; Westdeutsches Tumorzentrum Univ. Essen; KH Siloah Hannover; Maria Hilf II Mönchengladbach; Med. Univ. Tübingen; Westfälische Wilhelms-Univ. Münster; Kliniken Essen Mitte; Aventis Pharma Oncology, Bad Soden, Germany*

Purpose: The present study investigated Irinotecan as second line chemotherapy in patients (pts) with prior exposure to a weekly schedule of folinic acid 500 mg/m^2 i.v. followed by 5-FU 2.6 g/m^2 given i.v. over 24 hours for metastatic disease. Patients with histologically confirmed adenocarcinoma of the colon or rectum, measurable metastatic progressive disease and adequate bone marrow, liver and renal function were entered into the study after informed consent. Previous 5-FU based adjuvant CT and/or radiotherapy were allowed.

Methods: Irinotecan was given at a dose of 350 mg/m^2 (300 mg/m^2 for pts with WHO performance status of 2 and/or age > 70 years) i.v. over 30 min. every 3 weeks until progression of disease or occurrence of unacceptable toxicity.

Results: 111 pts. entered the study. 67 male, 44 female, median age 58 (33–84) years, median performance status 0 (0–2). After exclusion of 1 pt who never received treatment 110 pts were assessable for safety and 102 pts for tumor response. 110 pts received a total of 529 cycles of Irinotecan with a median no of 4 cycles per patient. The response rate was 11% [95% CI 5–17] and the NC rate was 65% [95% CI 54–79%]. The median time to progression and median survival were 4 and 9 months. 9% responses, and 65% NC were obtained in 96 pts with resistant disease. 2 PR and 4 NC were achieved in 6 pts with progressive disease between 4 to 12 months after end of first line CT. NCIC-CTC grade 3/4 toxicities included neutropenia 39% of pts., thrombopenia 2%, delayed diarrhea 20%, infection 7%, fatigue 7% and elevation of bilirubin 10%.

Conclusion: In case of failure of infusional modulated 5-FU, Irinotecan had considerable efficacy and an acceptable safety profile. The efficacy of Irinotecan in the present study is comparable with that obtained in other phase II studies using various 5-FU based regimen as first line CT. These results indicate that the efficacy of Irinotecan in second line treatment is widely independent of the previously used 5-FU based regimen.

1082 POSTER

Activity and safety of capecitabine and irinotecan (CPT-11) in association as first line chemotherapy in advanced colorectal cancer (ACRC)

E. Bajetta[1], D. Cortinovis[1], A. Cassata[1], S. Siena[2], G. Cartei[2], G. Pinotti[2], L. Carreca[2], A. Lambiase[3]. *[1] Istituto Nazionale per lo Studio e la Cura dei Tumori, Medical Oncology Unit B, Milan, Italy; [2] I.T.M.O. Group, Milan, Italy; [3] Roche S.p.A., Monza, Italy*

Purpose: The primary endpoint of this multiinstitutional phase II study is to evaluate activity and tolerability of the combination of CPT11 + Capecitabine. Both drugs are active against ACRC with synergist cytotoxicity in preclinical studies.

Methods: Between July 1999 and March 2001, 102 pts with ACRC were enrolled and randomized to receive: arm A: CPT11 300 mg/m2 on day 1 every 3 weeks; arm B: CPT11 150 mg/m2 day 1 and 8 every 3 weeks; Capecitabine was administered in both arms at the dose of 1250 mg/m2 twice daily from day 2, for 14 days. Preliminary results are available about the first 47 consecutive pts enrolled in the trial. The main characteristics are: arm A 24 pts; Arm B 23 pts; M/F 23/24; median age 59 years (38-76); primary tumor: colon 30, rectal 17.

Results: 34 pts are valuable for response: 6 CR (A:2 B:4) and 15 PR (A: 11; B: 4) were achieved with an overall response rate of 61.7% (21/34). Fortyfour pts are valuable for toxicity. Grade 3-4 treatment-related toxicity observed per pts was: Arm A hand-foot syndrome (4), diarrhea (5), anemia (2) and neutropenia (1); Arm B nausea (3), diarrhea (4) and neutropenia (2). One drug-related death occurred for gastrointestinal toxicity in arm B. Thus, the dose of both drugs have been reduced as follows: CPT11, A: 240 mg/m2 day 1 q21, B: 120 mg/m2 days 1 and 8 q21; capecitabine twice daily 1000 mg/m2 from day 2 for 14 days q21.

Conclusions: The preliminary results suggest that the combination of capecitabine and CPT11 is clinically active. In order to improve the safety of the combination the schedule has been modified, with a better toxicity profile.

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Acute morbidity following short course preoperative radiotherapy in operable rectal cancer: identification of associated factors

A. Hartley[1], S. Giridharan[1], L. Gray[2], L. Billingham[2], T. Ismail[3], J. Geh[1]. *[1] Cancer Centre at the Queen Elizabeth Hospital, Clinical Oncology, Birmingham, United Kingdom; [2] CRC Institute of Cancer Studies, Statistics, Birmingham, United Kingdom; [3] University Hospital, Surgery, Birmingham, United Kingdom*

Introduction: Short course preoperative radiotherapy (SCPRT) (25Gy in 5 fractions over 1 week) has been shown to reduce locoregional recurrence and improve overall survival in operable rectal cancer. However, there are concerns regarding the toxicity of SCPRT. The aim of this study was to document the early complications (within 3 months) in patients receiving SCPRT and to identify the factors associated with acute morbidity.

Methods: All patients receiving SCPRT between 1 Jan 1998 and 31 Dec 1999 were included. Information on each patient including age, sex, radiotherapy (RT) technique (field dimensions, beam arrangement and energy), surgical details (time from starting RT to date of surgery, type of operation, in-patient stay and morbidity/mortality within 3 months), histology (Dukes stage and circumferential margin) were obtained. Univariate and multivariate analysis were performed on the above co-variates.

Results: One hundred and seventy seven patients referred from 8 centres were identified. Mortality at 30 days and 3 months was 6% and 8% respectively. Complications occurred in 38% of patients (wound 13%, pelvic sepsis 7%, anastamosis 6%, thromboembolic 4%, haemorrhage 3%, other 11%). Age (p=0.030), RT field length (p=0.027) and time to surgery (p=0.017) were significantly associated with an increased risk of complications on multivariate analysis.

Conclusions: Based on our results we would advocate surgery within ten days of commencing SCPRT. This recommendation is consistent with the protocols of the Swedish Rectal Cancer Trial and the ongoing MRC CR07 trial.

1084 POSTER

The addition of continuous infusion 5-FU to preoperative radiotherapy increases sphincter preservation in locally advanced low rectal cancer

C. Crane[1], R. Myerson[2], J. Skibber[1], E. Birnbaum[2], A. Singh[2], T. Phan[1], J. Picus[2], M. Lockett[2], S. Curley[1], N. Janjan[1]. *[1] MD Anderson Cancer Center, Houston, USA; [2] Wash U School of Medicine, St. Louis, USA*

Purpose: To compare the results of preoperative chemoradiotherapy (CXRT) to radiotherapy alone in two large, single institutional experiences.

Patient and Methods: Between 1978 and 2000, 455 localized, non-metastatic clinically staged T3 rectal cancer patients from two institutions were treated with preoperative radiotherapy. Patients at institution 1 (INT1, n=245) were treated with pelvic CXRT exclusively. They were compared to patients at institution 2 who were treated with pelvic radiotherapy alone (INT2a, n=144) initially, and CXRT (INT2b, n=66) more recently following a policy change. Both institutions used 45 Gy/25fx, while INT2 used 20 Gy/5fx in selected cases (n=20). Concurrent chemotherapy consisted of concurrent continuous infusion 5-FU 1500 mg/(m2-week) in both institutions. The endpoints were sphincter preservation (SP), relapse-free survival (RFS), and local control (LC).