2 g/m^2 in case of no toxicity > grade 2. 40 pts have been evaluated: 25 M/15 F, mean age 60 yrs, liver metastasis 33 pts, lung 11, peritoneal 4, other 11, multiple 13, performance status (WHO) 0: 20, 1–2: 20. Previous chemotherapy consisted in different optimal FA-5FU modulations ± hydroxyurea. 16 previously received the same high-dose FA and 5FU CI regimen alone or with interferon-α. All pts had disease progression on first-line therapy for metastatic disease or < 6 months after adjuvant therapy. One CR, 18 PR (response rate 49%), 17 stable (44%), and 3 prog. (8%) were observed (1 non-evaluable pt). Nine pts who progressed on the same high-dose FA and 5FU CI regimen responded (56%). From start of FOLFOX, median PFS was 9.6 mths, 12-mth median survival 65%. WHO toxicity ⩾ grade 2 was: acro-syndrome or neuropathy 28% pts (g 3: 8%), nausea 28% (g 3: 3%), diarrhea 36% (g 3: 8%), mucositis 31% (g 3: 11%), neutropenia 42% (g 3–4: 28), thrombopenia 17% (g 3–4: 8%), alopecia 28% (g 3: 8%), allergy 3%. 17 pts (42%) experienced grade 3–4 toxicity. This high-dose intensity schedule achieves a high response rate in pretreated metastatic CRC even in pts who had received the same high-dose FA and 5FU CI regimen. Limiting toxicities are neutropenia and neuropathy.

717 POSTER

DOES HIGH-DOSE PRE-OPERATIVE RADIOTHERAPY ALTER THE STRENGTH OF COLON ANASTOMOSIS IN RATS?

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The purpose was to study the effect of pre-operative radiotherapy on the strength of colon anastomosis, constructed of one irradiated and non-irradiated segment, as well as the difference between a conventional and a hyperfractionated radiation treatment.

Groups of 15 animals were treated with conventional (2.0 Gy/day to total doses of 40.0, 60.0 or 80.0 Gy) or hyper-fractionated (1.6 Gy, 2×/day to total doses of 41.6, 60.8 or 80.0 Gy) radiotherapy and compared to control and sham treated groups. The strength of the colon anastomosis (constructed the day after ending the radiotherapy) was measured by a bursting experiment. End results were bursting pressure (BP) and bursting wall-tension (BWT).

There was no significant difference in BP or BWT between the irradiated animals and the control groups.

We conclude that high-dose pre-operative radiotherapy to one end of a colon anastomosis does not affect its anastomotic strength.

718 POSTER

PREOPERATIVE VERSUS POSTOPERATIVE RADIATION THERAPY FOR RESECTABLE RECTAL CANCER

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Purpose: To compare the results of preoperative and postoperative radiotherapy in adenocarcinoma of the rectum in terms of survival and control of disease.

Patients and Methods: From 1989 to 1993, 52 patients with clinically operable rectal cancer were treated in our department: 25 patients in Group I (pathologic stage B2, B3 or C) received postoperative radiotherapy 50 Gy, and 27 patients in Group II received preoperative radiotherapy 30 Gy. All patients had a Karnofsky index greater than 60% and no evidence of distant metastases.

Results: With a median follow-up of 40 months, the overall 5-year actuarial survival was 75% in Group I and 83% in Group II, and the 5-year disease-free survival 52% and 83% respectively ($P = 0.025$). Pathologic complete response was found in one case in Group II, and preservation of the anal sphincter was possible in an increased number of cases (16 patients) in this group.

Conclusions: We observed better results with preoperative radiation therapy and would recommend this treatment for rectal carcinoma.

719 POSTER

DOXIFLURIDINE IN ADVANCED COLORECTAL CARCINOMA. PARALLEL MULTICENTRE RANDOMIZED PHASE II TRIAL

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Doxifluridine (5-dFUR) is a fluoropyrimidine derivative with a better therapeutic index than FU (Bajetta, *Eur J Cancer*, 1993). This study independently evaluated the activity of two different schedules of oral or i.v. 5-dFUR plus levo-leucovorin. Between April 1993 and September 1994, a total of 130 untreated (in an adjuvant and metastatic setting) pts with measurable colorectal cancer were randomized to 5-dFUR 750 mg/m^2 p.o. on days 1→4 and levo-leucovorin 25 mg/dose p.o. two hours before 5-dFUR, repeated every 12 days (Arm A); or 5-dFUR 3000 mg/m^2 as a one hour i.v. infusion for 5 consecutive days combined with levo-leucovorin 25 mg/dose i.v. immediately before 5-dFUR every 21 days (Arm B). The first response evaluation was made after 2 mos of treatment. The two arms were well balanced in terms of age (median 61 yrs, range 31–80), sex (M/F: 69/61) and disease extension. A preliminary intent-to-treat analysis was made of 126 adequately treated pts (4 too early to evaluate), of whom 67 were in Arm A and 59 in Arm B. The response rates were 15% in Arm A (2 CR, 8 PR, 29 SD, 28 PD) and 39% in Arm B (5 CR, 15 PR, 15 SD, 21 PD). Toxicity included WHO grade 3 and 4 diarrhea in respectively 16% and 7% of Arm A and 16% and 15% of Arm B respectively. Mucositis was mainly observed in Arm B (grade 3 in 13% and grade 4 in 1%). The preliminary data confirm the good tolerability profile of both the oral and the i.v. schedule. The oral route seems to be promising and is interesting, because it could be benefit for pts suitable for home treatment. Moreover, this study confirms the efficacy of i.v. doxifluridine as a fast line therapy in advanced colorectal cancer. *Data management by I.T.M.O. (Italian Trials in Medical Oncology) Scientific Service.*

720 POSTER

5-FLUOROURACIL (FU) AND LEVAMISOLE (LEVA) VERSUS FU, LEVA AND 6-S-LEUCOVORIN (6-S-LV): AN ITALIAN INTERGROUP STUDY OF ADJUVANT THERAPY FOR RESECTED COLON CANCER (B2-C)

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In order to determine whether the addition of 6-S-LV to the combination FU + LEVA reduces the rate of recurrence and prolongs DFS and OS in patients with radically resected colon cancer, Dukes' stage B2–3, and C we conducted a large scale randomized clinical trial accruing patients from five Italian cooperative groups. After stratification for center, treatments were as follows: ***arm A, 5FU 450 mg/sqm iv d 1–5 + LEVA 150 mg po d 1–3; arm B, 6-S-LV 100 mg/sqm iv d 1–5, FU 370 mg/sqm iv d 1–5 + LEVA*** *given as arm A.* In both arms courses were repeated every 28 days × 6 cycles. A minimum sample size of 725 pts. per arm was set to ensure an 80% probability (α *error* .05) of detecting a 20% reduction in overall mortality at 5 yrs, calculated on the basis of the experimental group. The study was activated in March 1992 and was closed in February 1995, 1827 pts. were accrued with a monthly accrual of 51 pts. At December 1994, 54% of these pts were men and 46% women with median age 63 yrs (range 26–84) and median PS 0 (0–1). Forty-seven percent had B2–3 Dukes while 53% C. The sites of the resected tumors were: ascending colon (29%), transverse (16%) and descending (55%). There were 4 toxic deaths: 1 in the arm with LV (diarrhea with dehydration) and 3 in the control arm (neutropenia-related septic shock diarrhea with dehydration). Severe toxicity (gr 3–4 WHO) was observed in 18% of pts. in arm A and 31% in arm B.

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