in those without (median IL-6=2.3 pg/ml $p<0.05$; median sE-selectin=42.0 ng/ml, $p<0.005$). Moreover 85% of patients without distant metastases had sE-selectin levels <70 ng/ml, whereas 50% of metastatic patients had sE-selectin levels >70 ng/ml (Chi-square: 5.8, $p<0.02$).

Conclusions: The results obtained showed that IL-6 and sE-selectin levels are associated with elevated CA 19-9 levels and the presence of metastatic disease, suggesting that these molecules may play an important role in the haematogenous metastasis of colorectal cancer.

1138 POSTER

Phase II evaluation of an alternated FOLFOX/FOLFIRI regimen in patients with resistant metastatic colorectal cancer (CRC)

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Oxaliplatin (LOHP), irinotecan (CPT 11) and 5 FU are active chemotherapeutic agents in patients with metastatic CRC. The use of LOHP is frequently limited by the occurrence of a cumulative neurotoxicity. Furthermore, CPT11 may interfere with DNA repair in tumor cells after exposure to oxaliplatin. To avoid the occurrence of the LOHP-related neurotoxicity, and to assess a potent synergy between LOHP and CPT11, we evaluated an alternated combination of FOLFOX and FOLFIRI regimens in patients with metastatic CRC after failure of a first line 5FU-leucovorin association. Patients alternatively received 4 courses of FOLFOX 6 (LOHP 100 mg/m2 d1 + simplified LV5FU2, repeated every 2 weeks) and 4 courses of FOLFIRI (CPT11 180 mg/m2 d1 + simplified LV5FU2, repeated every 2 weeks) until disease progression or limitant toxicity. Thirty eight patients were enrolled: M/F = 23/16, median age 64 (28-78), PS 0/1/2: 26/10/2. All patients were evaluable for toxicity, and 31 were evaluable for efficacy. Main results are presented here:

(1) Toxicity (grade 3-4) (NCI-CTC) (n = 38)
- Neurotoxicity*: 2 (5.2%)
- Neutropenia: 7 (18.4%)
- Febrile neutropenia: 0
- Diarrhea: 5 (13.1%)
- Alopecia 1 (2.6%)

(2) Efficacy (n = 33)
- OR/SD/PD (%) (WHO): 18 (54.5)/11 (33.3)/4 (12.1)
- Median TTP (months)**: 7.1
- Median survival (months)**: 14.4

*Specific scale, Levi et al. ** Current values, final results will be available at the meeting.

The evaluated alternated combination is well tolerated, specially with unfrequent neurotoxicity. Furthermore, the results suggest a potentiation between LOHP and CPT11, with interesting OR rate, TTP duration and survival.

1139 POSTER

Neo-adjuvant concomitant chemo-radiotherapy with dose intensification in UT3 rectal tumour

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The aim of the study is to evaluate the efficacy of an intensive neo-adjuvant chemo-radiotherapy schedule, in order to gain a better down-staging in staged uT3 rectal tumours.

From 4/99 to 3/01 65 patients (pts) entered the study. Median age was 61 yrs; the median distance from the anal verge was 4.6 cm; the gross tumours median extension was 5.1 cm. Pre-therapy clinical staging found out: 48% of cases uT3N-, 52% of cases uT3N+. All patients were staged also with endorectal ultrasonography The radiation therapy schedule delivered different doses at different volumes: 46-48 GY to posterior pelvis; 51 Gy to total mesorectal space, and 54 Gy to neoplastic volume. The concomitant chemotherapy was administrated with 5-Fluorouracil at dose of 300 mg/m2/day (7 days/week) by continuous infusion along 32 consecutively days. Surgery was performed 8 weeks after the end of chemo-radiation-therapy: 57 pts underwent surgical procedure, 8 pts are still waiting for intervention.

Pathological stage was: 40%, 18%, 12%, and 28% in stage 0, I, II and III, respectively; the global down-staging rate was 67.%. Pathologic complete remission (pCR) was obtained in 26% of cases; the rate of only microscopic disease (pTmic) was 16%. Gross tumour extension was correlated with pathological response: downstaging, pCR, and pTmic were, for tumours < 5 cm vs tumours = 5 cm, equal to 76% vs 62%; 40% vs 19%; 24% vs 13%, respectively. All pts were resecated, conservative surgery was possible in 78% of all cases; in 90% of pCR or pTmic pts. Gastro intestinal and haematological G3 (RTOG score) toxicity incidence was 4% and 7%, respectively. Peri-operative morbidity was joined in 16% of cases.

Neo-adjuvant concomitant chemo-radiotherapy with dose intensification (as proposed) may be efficacy in obtaining high rates (about 60%) of major pathologic responses (0-1 stages), with moderate toxicity.

The study is going on.

1140 POSTER

Topoisomerase-1 (topo-I) and thymidylate synthase (TS) primary tumor expression as prognostic and predictive factors for response to cpt-11 in advanced colorectal cancer (crc) patients

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CPT-11, a DNA topo-I inhibitor, has demonstrated antitumor activity in CRC patients in first-line therapy and after failure of 5-FU/LV- based chemotherapy. Previous reports suggest that TS expression could be considered a predictive factor for CPT-11 treatment (Saltz L. et al, ASCO 1998; 17:281a. In order to evaluate the clinical relevance of both Topo-I and TS, we analysed the primary tumor expression by IHC assay of Topo-I (NCL-Topo-I mAb) and TS (TS106 mAb) in a series of 50 patients with advanced CRC receiving CPT-11 based chemotherapy regimen. Thirty-two percent and 58% of cases were considered positive for Topo-I and TS expression, respectively. Patients with different Topo-I (32% vs 40%, respectively) and TS status (25% vs 42%, respectively; p: n.s.,) did not show a significant different probability of response to treatment. The best predictive pattern was demonstrated when TS and Topo-I tumor expression were considered together. In fact, while Topo-I -/TS - cases showed 28% of objective response rate (ORR), all the remaining subgroups showed an overall 41% of ORR. Moreover, while TTP resulted not related with the above bio-markers, OS resulted significantly associated with Topo-I tumor status ($p< 0.05$). The multivariate analysis confirmed for Topo-I tumor status a significant and indipendent role either on TTP or on OS ($p< 0.04$ and $p< 0.01$, respectively. In conclusion, our data suggest that Topo-I and TS primary tumor expressions could have clinical relevance prevalently on long term prognosis for CPT-11 treated patients with advanced CRC.

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1141 POSTER

Rectal cancer: quality of life during radiation therapy

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Purpose: The purpose of the study was to investigate whether health-related quality of life (QoL) was reduced during radiation therapy for rectal cancer.

Methods: This was a prospective study of 58 patients. Thirty-six patients received preoperative radiation therapy for locally advanced or recurrent rectal cancer. Twenty-two patients received postoperative adjuvant radiation therapy with concomitant chemotherapy (5-FU/leucovorin) for operable rectal cancer. All patients were treated with 2 or 3-field box technique, 50 Gy in 2 Gy fractions. QoL was assessed with the core questionnaire EORTC QLQ-C30 and the colorectal cancer module EORTC QLQ-CR38, scores were transformed to a scale from 0 to 100. A 5-day diary was also completed, including frequency of defecation and items from the common toxicity criteria (CTC). QoL and toxicity were assessed at start of treatment, end of treatment, and 4-6 weeks later.

Results: During radiation therapy, fatigue and diarrhoea were significantly increased, fatigue from 33 to 44 ($p<0,001$), and diarrhoea from 26 to 46 ($p=0,001$). Gastrointestinal problems increased from 18 to 26 ($p<0,001$). Overall QoL and several other scales showed significant, but small changes (less than 10 on a scale from 0 to 100). One month after completion of radiation therapy, QoL scores had returned to pre-treatment values. QoL scores during treatment will be related to CTC scores, and to the QoL of the general Norwegian population.