11(13%) patients and more than 90% necrosis was observed in additional 14 patients(18%). After a median follow-up of 36 months, survival and overall survival rates of the resected patients were 95%, 69% and 86% respectively.

Conclusion: The pre-operative chemo radiation regimen employed had a tolerable acute toxicity profile. It is a reasonable option in patients who have locally advanced or lower 1/3 rectal cancer and with low locoregional recurrence.

1134 POSTER

COX-2 expression in rectal cancer: immunohistochemical pattern and prognostic value

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Purpose: It is controversial whether COX-2 expression is a prognostic factor for rectal cancer with respect to other established prognostic parameters for local recurrence and/or survival in this disease.

Methods: To evaluate the impact of COX-2 on outcome of rectal cancer we reviewed data of 62 patients with adenocarcinoma of the rectum treated between 1995 and 1996, all patients in stage I-III were resected curatively. The samples were stained for COX-2 expression using a polyclonal antibody for human COX-2. According to the intensity and extend of positive reaction of tumor cells the labeling index of stained cells was calculated.

Results: The median labeling index was 0.58. The chi-square-test revealed no correlation between COX-2 and the established prognostic factors. In the univariate analysis COX-2 overexpression did not show a significancy according to the endpoints local recurrence ($p=0.41$) or disease specific survival ($p=0.28$). In contrast COX-2 was a significant prognostic factor for pulmonary metastasis ($p=0.04$).

Conclusion: The majority of specimens showed a mild or moderate immunoreactivity for COX-2 but there is a lack of significancy for COX-2 expression as a prognostic factor for local control and survival. However, there is evidence that COX-2 overexpression might be linked to an increased risk for hematogenous metastatic spread.

1135 POSTER

Irinotecan (CPT-11) plus oxaliplatin (LOHP) plus infusional 5-fluorouracil (5-FU) and leukovorin (LV) as first line treatment for metastatic colorectal cancer (MCC): A phase II trial

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Background: A phase II study was conducted in order to evaluate the toxicity and efficacy of the combination of CPT-11 plus LOHP plus infusional 5-FU/LV in MCC.

Patients and Methods: Thirty-five chemotherapy-naïve patients were enrolled. The median age was 60 y; male/female: 21/14; PS (WHO) 0/1/2: 16/14/5; prior surgery 24 pts; adjuvant chemotherapy: 18 pts; adjuvant RT: 3 pts; Number of metastatic sites 1/2/≥3: 13/12/10. CPT-11 was administered on d_1 at the dose of 150 mg/m^2 over a 90 min infusion, LOHP on d_2 at the dose of 65 mg/m^2 over a 2 h infusion, simultaneously but in different lines with LV (200 mg/m^2 on days 2 and 3) followed by 5-FU administration as bolus iv infusion at dose of 400 mg/m^2/d and as 22 h continuous infusion at the dose of 600 mg/m^2/d on days 2 and 3. The regiment was repeated every 2 weeks.

Results: All patients were evaluable for toxicity and 28 (5 too early, 2 not evaluable) for response. CR was achieved in 2 pts (7.1%) and PR in 14 pts (50%) (ORR: 57.10%; 95 ci: 39,12%–82.64%); 9 pts (32.1%) had SD and 3 (10.7%) PD. The median duration of response was 4.5 m; the median TTP and OS have not yet been reached, after a median follow up period of 11 months. Grade 3 and 4 neutropenia occurred in 12 pts (34.29%), febrile neutropenia in 2 pts (5.7%), anemia grade 2 in 5 pts (19%), while thrombocytopenia didn't exceed grade 1. Diarrhea grade 3/4 was observed in 10 pts (28.5%), neurotoxicity grade 3/4 in 3 pts (8.5%), asthenia grade 3 in 2 pts (8.5%). No treatment related death occurred.

Conclusions: The combination of 5-FU/LV + CPT-11 + LOHP is an active and well-tolerated regiment as front-line treatment in MCC and merits further evaluation in prospective randomized trials.

1136 POSTER

Joint United States of America (USA)/Japan study of UFT (uracil and tegafur) plus leucovorin (LV) in patients (pts) with metastatic colorectal cancer (CRC)

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Introduction: UFT is a 5-FU prodrug developed as a single agent against various solid tumors in Japan. Based on the extensive use of LV with 5-FU in the West, UFT was combined with LV for the treatment of CRC in the USA and European countries. Two large phase III study demonstrated equivalency between intravenous 5-FU/LV and UFT/LV among Western patients with CRC (Pazdur R., and Carmichael J., ASCO 1999). Although different doses and schedules of UFT in CRC have been tried in Japan, there is no study with the combination of UFT plus leucovorin in that Country.

Methods: To evaluate the applicability of the results of the large Western trials to the Japanese population we decided to compare the response rates, the PK, and the type, frequency, and severity of side effects in American and Japanese pts with metastatic CRC.

Results: A total of 99 pts (45 in USA; 44 in Japan) has been enrolled; all are evaluable for toxicity and 98 pts are evaluable for response. Both groups were well matched for gender, age, performance, and prior adjuvant treatment. As of now, results show a comparable response rate of 36% and 34% in Japan and the USA, respectively. Diarrhea was the main toxicity in both groups and severe diarrhea was seen significantly less often among Japanese pts (9% versus 22% in the USA). Hematological toxicity was very mild and not significantly different in both groups. There were no other significant differences in toxicity. This indicates that UFT/LV is equally active in both ethnic groups but potentially more toxic among Western pts. Although AUC and Cmax of FT, 5-FU and Uracil were slight higher in Japanese pts than in the USA, when the results are adjusted for BSA, the parameters are similar.

Conclusion: The present study indicated that UFT/LV therapy is an equally efficient and reasonably well-tolerated treatment for American and Japanese pts with metastatic CRC. This data indicates that an extrapolation of clinical data from the West to the East is reasonable.

1137 POSTER

Serum concentration of soluble adhesion molecules and cytokines in patients with colorectal cancer

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Purpose: Human colorectal cancer cells express sialyl Lewis (a)(CA 19-9), which acts as a ligand for E-selectin, an adhesion molecule involved in the binding of colorectal cancer cells to endothelial cells. Circulating levels of inflammatory cytokines have been associated with the disease status of cancer patients. Moreover, IL-6 has been associated with CA 19-9 levels in patients with colorectal cancer. Therefore, this study was aimed to verify whether tumor marker levels correlate with blood concentrations of cytokines and adhesion molecules involved in the haematogenous spread of colorectal cancer cells.

Methods: Serum tumor markers (CEA, CA 19-9, CA 72-4), cytokines (TNF-alpha, IL-6, IL-1beta) and soluble adhesion molecules (sP- and sE-selectins, sVCAM) levels were measured in serum samples from 76 patients with primary (Stages: A=6, B=34, C=19, D=2) or recurrent (local=3, distant=12) colorectal cancer.

Results: Median cytokine levels were higher in cancer patients (TNF: 13.8 pg/ml; IL-1: 0.5 pg/ml; IL-6: 2.4 pg/ml) compared to controls (TNF: 0.3 pg/ml; IL-1: 0.1 pg/ml; IL-6: 0.2 pg/ml) (all $p<0.001$). Moreover, mean (SD) sE-selectin and sVCAM levels were higher in cancer patients [sE-selectin: 56.2 (32.5) ng/ml; sVCAM: 985 (509) ng/ml] compared to controls [sE-selectin: 39.3 (14.8) ng/ml, $p<0.01$; sVCAM: 478 (239) ng/ml, $p<0.001$]. Plasma sP-selectin levels did not show any significant difference. IL-6 levels directly correlated with sE-selectin ($r=0.40$, $p<0.01$) and sVCAM ($r=0.48$, $p<0.002$), and sE-selectin directly correlated with sVCAM ($r=0.43$, $p<0.006$). Patients with sE-selectin >70 ng/ml [mean (2SD) of controls] also had higher levels of CA 19-9 ($p<0.0005$), CEA ($p<0.002$) or CA 72-4 ($p<0.02$). IL-6 and sE-selectin levels were higher in patients with metastasis (median IL-6=5.5 pg/ml; median sE-selectin=71.5 ng/ml) than