and 88% for FA. Overall response on 68 evaluable pts: 7 CR (10%), 19 PR (28%), 15 MR (22%), 16 SD (24%) and 11 PD (16%) have been reported. Median time to progression: 6.6 months and median duration of response: 11.1 months. The combination is well tolerated with G 3/4 diarrhea (pt/cy) of 15%/1% and G 3/4 neutropenia (pt/cy) 68%/20%. Febrile neutropenia was reported in 2 pts and G3/4 infection with neutropenia in 7 pts. Only 5% of the cycles were administered with a reduced dose. This combination appears to be very promising with a good benefit risk/ratio. A phase III is ongoing to compare this regimen to the reference CPT-11 combined with 5FU/FA de Gramont schedule.

1130 POSTER

CPT-11 and 5 fluorouracil/folinic acid (5-FU/FA) mayo clinic regimen in advanced colorectal cancer (CRC) as front line therapy: a phase I/II study

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CPT-11 combined with 5- FU either infusional or bolus is the new reference regimen in front line treatment of CRC. Mayo clinic bolus (b) regimen is also widely used in this setting. The combination of CPT-11 combined with Mayo clinic regimen has been assessed in a phase I/II. CPT-11 was administered as 30-90 min IV infusion, day 1 immediately followed by FA 20mg/m2 15 minutes followed by 5-FU at a fixed dose of 425mg/m2 IV, 15 min, from day 1 to day 5 every 4 weeks. Two dose of CPT-11 were tested in phase I: level 1: 250 mg/m2, level 2: 300 mg/m2. Major inclusion criteria: measurable lesion, no previous chemotherapy for advanced disease, WHO performance status less or equal to 2. Twenty-three patients have been treated in phase I, 14 males/9 females. Median age is 58 (30-69), median organ involved 2 (1-4). 43 cycles (cy) and 63 cy were administered at level 1 (10 patients, pts) and 2 (13 pts) respectively. RDI of CPT11/5-FU/FA was 94.0% for each compound and for both levels. At first cycle, dose limiting toxicities at level 2 were: diarrhea grade 4 (4 pts). Overall, main grade 3-4 toxicities were diarrhea (4pt/5cy) at level 1 and 6pt/9cy at level 2, neutropenia (5pt/6cy) at level 1 and (7pt/15cy) at level 2. Three partial responses were observed at each dose level. The recommended dose was defined as CPT-11 250 mg/m2. Efficacy is promising and safety is manageable. The combination was assessed in phase II: 50 patients have been treated at RD. Preliminary results will be presented at the meeting.

1131 POSTER

Radiotherapy of inoperable recurrent rectal carcinoma

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Purpose: Radiotherapy (RT) is the treatment of choice for inoperable locoregional recurrent rectal carcinoma (ILRCR). The aim of this work was to present that radical doses of RT as well as different RT techniques influence overall response rate (ORR) and overall survival (OS) in this group of patients (pts).

Methods: From 1995 till 2000, at the Institute of Oncology and Radiology of Serbia, Belgrade, 60 pts had been treated for ILRCR, median age 60 years (37-76), male:female ratio 1:1,4. There were 26 pts with Dukes B stage, 30 pts with Dukes C stage while 4 pts had unknown primary stage. Abdominoperineal resection was the most common initial therapy (in 65% of pts) with median disease free survival (DFS) of 24 months (12-60). The sites of recurrent disease were: presacral (21 pts), presacral and vaginal (18 pts), presacral and perineal (11 pts), vaginal (7 pts), at anastomosis (2 pts) and 1 perineal. Each pt was treated with radical RT doses. External beam RT (EBRT) was solely applied in 35 pts, 3 and 4 fields technique and doses of 50-62 Gy. Combined EBRT and brachitherapy (BHTH) was applied in 25 pts. EBRT doses were 30-65Gy and BHTH doses 12-40Gy. Acute skin RT complications were notified in 29 pts (48%) of GI and GII.

Results: The ORR was registred in 40/60 pts (66%) (CR-33%, PR-33%) and was estimated 2 months following RT. The median follow-up time was 19 months (8-60) and 27 pts (46%) had disease free, 7 pts (12%) residual disease, 4 pts stable disease, 15 pts local progression (25%), 6 pts distant progression and 1 pt was lost. There was 38 pts (63%) alive and 22 pts had died (37%). In the group of complete responders (20 pts), 3 yrs DFS was 63,92% and 3 yrs OS 84,85%. Among treated pts (60) there was 3 yrs DFS of 41,14% and 3 yrs OS of 55,11%.

Conclusion: The radical doses of RT improved the local control and OS. We find that there was not statistically significant difference between different RT techniques (EBRT and EBRT+BHTH) regarding DFS and OS.

1132 POSTER

Serum levels and tumor expression of HER-2 in colorectal cancer (CRC) - a prospective analysis

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Rationale: The oncogene HER-2 is overexpressed in 20-25% of breast and ovarian cancers and is the target for novel therapeutic strategies with monoclonal antibodies or small molecules. Reports on the expression levels of HER-2 in CRC have been inconsistent, potentially due to differening methods of detection. Recently, soluble HER-2 has been characterized in the serum of patients with various carcinomas, however the correaltion between tumor expression of HER-2 and respectibe HER-2 serum levels is still unknown. Therefore, we prospectively analyzed sera and tumor samples of patients with metastatic CRC for the expression of HER-2 using standard ELISA and immunohistochemistry (IHC) techniques and tried to correlate it with the clinical course of the disease.

Patients and Methods: Serum levels of HER-2 were determined in 88 pts (52 m, 36 f) with metastatic CRC and 20 healthy controls using a commercially available ELISA system (Dako). In 46 pts, tumor expression of HER-2 was analyzed by IHC (Hercept-Test®, Dako). Routine lab parameters and tumor markers CEA and CA19-9 were recorded in all patients.

Results: HER-2 serum levels were significantly higher in pts with CRC compared with the control group (mean 2511 vs. 2184 U/ml; p=0.038). 21 of 88 pts (23.9%) showed elevated serum levels (>3000 U/ml), but in only 6 of 46 pts (13%) weak expression of HER-2 could be detected in tumor samples (2x 1+, 4x 2+, 0x 3+ Dako-score!). However, a positive correlation could be found between serum levels and tissue expression of HER-.2 (p=0.035). HER-2 serum levels were further significantly correlated with CEA (p=0.031), bilirubin (0.04) and with ongoing anti-tumor therapy (p=0.0083), but not with CA19-9, CRP, LDH, creatinine, hematological parameters (Hb, leukocytes, platelets) and age. Patients with liver metastases were more likely to demonstrate elevated serum levels of HER-2 (p=0.0033), but did not show HER-2 overexpression in the respective primary tumors. In preliminary analysis, HER-2 serum levels did not correlate with overall survival.

Conclusions: Very few colorectal cancers overexpress HER-2 when assessed by standard IHC. Therefore,molecular approaches targeting this oncogene in CRC are not necessarily warranted. The pathophysiological role of elevated levels of soluble HER-2 in the serum of a substantial number of patients with CRC has yet to be determined. Supported by a research grant from Hoffmann-La Roche.

1133 POSTER

Preoperative 5FU and mitomycin-c with concomitant radiotherapy for locally advanced rectal cancer

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Purpose: Investigate the effectiveness and toxicity of pre-operative chemoradiation for adenocarcinoma of the rectum.

Methods: Eight-six patients were assessed. Pre-Operative pelvic radiotherapy was delivered in three or four fields. 50~50.4Gy in 25~28 fractions over 5 weeks. Concurrent chemotherapy with mitomycin C at 10 mg/m2 on day 1 and continuous infusion of 5-fluorouracil (5-FU) at 1000mg/m2/day on days 1~4 and days 29~33 was delivered to the patient during radiotherapy. Total mesorectal excision of the rectal tumor either by anterior or abdomino-perineal resection was planned at 6~8 weeks from completion of pre-operative radiotherapy. Response to therapy was assessed by microscopic measurement of the surgical specimen.

Results: All 86 patients undergoing chemotherapy and radiotherapy completed therapies as planned, with no treatment-related interruptions. Nine patients refused to have surgery. Grade 3 or more diarrheas was observed in 36(42%) patients, leukopenia 17(20%), and infection 4(5%) patients. Anal preservation rate in patients whose tumor located within 5 cm to anal verge was 86%. Complete pathologic remission was observed in