1-2 in 44, gr. 3 in 6 and gr. 4 in 4) and 34 pts (29.8%) cutaneous toxicity (gr. 1-2 in 29 and gr. 3 in 5). All patients underwent surgery after a median interval of 43 days from completion of adjuvant therapy. Surgical procedures were: low anterior resection in 92 (80.7%) and abdominoperineal resection in 22 (19.3%). Downstaging was obtained in 76 pts (66.6%) while complete pathological response was found in 18 (15.7%). No early mortality due to adjuvant or surgical treatment was found. Major postoperative complications occurred in 22 pts (19.3%): 7 clinical anastomotic leaks, 3 pelvic abscesses, 5 delayed perineal wound healing, 2 rectovaginal fistulas, 1 stoma ischemia and 4 postoperative ileus. After a median follow-up of 24 months (range 5-86), 4 (3.5%) local recurrences and 24 (21%) distance metastasis were observed. Eighty-eight pts were alive and disease free and 12 were alive with distance metastasis. Fourteen had died (12 of cancer related causes and 2 of other causes).

Conclusions: Local control compared favourably with recently published data. A high rate of downstaging and sphincter saving were obtained with acceptable toxicity, however a longer follow up is necessary to verify the impact on survival.

1096 POSTER

Relationship between high dose irinotecan (260mg/m2) and response rate, without increased toxicities in metastatic colorectal cancer (MCRC) combination with bi-weekly 5FU/FA in a phase II study

M. Ducreux[1], J. Raoul[2], Y. Merrouche[3], P. Marti[4], M. Risse[5], D. Mery-mignard[5], O. Ferment[5], V. Boige[1]. [1] *Gustave Roussy, Gastroentérologie, Villejuif, France;* [2] *Eugene Marquis, Gastroentérologie, Rennes, France;* [3] *CHU Jean Minjoz, Radiotherapie, Besançon, France;* [4] *clinique Marzet, Pau, France;* [5] *Aventis, Paris, France*

The recommended dose of irinotecan with LV5FU2 is 180 mg/m2. In this phase I study the MTD was 300 mg/m2. In monotherapy, level 500 mg/m2 was safe in 2/3 patients(pts) with good response rate. The rationale of this study is to confirm safety and efficacy irinotecan 260 mg/m2 combined with LV5FU2 (group 1) then with LV5FU simplified regimen (group 2) after better safety published results of this schedule. The primary endpoint is the ORR.

Results: 34 pts with MCRC (10 had received adjuvant chemotherapy) were included for 1rst line, prophylactic G-CSF after hematological toxicity to maintain dose intensity; sex ratio (H/F)=20/14; median age 55y[41-73]; PS 0/1=16/18; number of sites involved 2[1-4].

	Group 1 (%cy/%pts)	Group 2 (%cy/%pts)
N cycles/N patients	209/20	46/14
Median cy/patients	8.0 [1-16]	5.0 [1-8]
Diarrhea G3/G4	(1.0/4.2)/(0/0)	0/0
Asthenia G3	1.5/13	4/10
Vomiting/Nausea G2	(2.5/17)/(5/21)	(6/20)/(10/30)
Neutropenia G3/G4	(15/58)/(2/21)	(17/60)/(0/0)
Febrile neutropenia	0.5/5	0/0
ORR (%RP-SD-PD)	(20 pts) 55*-35-10	Too early**

*3 pts with surgical resection of liver metastases. **Only one evaluation per patient.

Conclusion: Preliminary results, CPT-11 260mg/m2 demonstrates a good safety profile, more especially when combined with simplified LV5FU than LV5FU2, with an overall better efficacy when compared to 180 mg/m2.

1097 POSTER

Significance of different classes of p53 gene mutation in patients with colorectal cancer

C. Belluco, R. Bertorelle, M. Forlin, L. Chieco-Bianchi, D. Nitti, M. Lise.

Purpose: The p53 tumor suppressor gene controls many critical processes related to tumor development and progression. Specific p53 mutations have been found to be associated with various clinical phenotypes. The clinical and pathological significance of p53 mutations in defined structural and functional domains were prospectively investigated in a large series of colorectal cancer patients.

Methods: Surgical specimens from 335 consecutive patients with stage I-IV colorectal adenocarcinoma were collected between 1991 and 1998. p53 gene mutations in exons 4 to 8 were searched for by PCR-SSCP analysis, followed by direct DNA sequencing. Comparison between groups was made using the Chi-square test. Survival analyses were carried out by the log-rank test and the Cox's proportional hazards model.

Results: p53 gene mutations were detected in 141/335 (42.1%) cases. The higher mutational frequencies were found in exons 5, 7 and 8 (37.6%, 24.8% and 29.1% respectively). p53 gene mutations were associated with left-sided tumors ($p<0.001$) and more advanced lesions (stage III and IV) ($p<0.01$). In particular, mutations located on exon 5 and in the L2 loop region were significantly associated with tumors in stage III and IV. At univariate analysis of survival, no significant differences were found in relation to p53 gene status. However, among cases with p53 gene mutations, those with alterations in exons 4 to 6 had a worse outcome than those with alterations in exons 7 and 8 ($p<0.02$). On the other hand, cases with L3 loop region mutations had a better outcome than cases with mutations in other sites of the gene ($p<0.05$). At multivariate analysis, the only factors which independently predicted survival were tumor site and stage.

Conclusion: Our results indicate that p53 gene mutation is not a prognostic marker in patients with colorectal cancer. Specific p53 gene mutations in defined structural and functional domains are associated with different clinical and pathological findings.

1098 POSTER

Colorectal cancer (CRC) patients surveillance with virtual computed tomography colonography(CTC): preliminary results

E. Bria[1], L. Trasatti[1], G. Larosa[1], C. Capalbo[1], I. Carbone[2], R. Iannaccone[2], A. Laghi[2], S. Lauro[1], A. Vecchione[1]. [1] *Policlinico "S. Andrea", Medical Oncology, Rome, Italy;* [2] *Policlinico "Umberto I", Institute of Radiology, Rome, Italy*

Purpose: Which is the best follow-up schedule in colorectal cancer (CRC) patient is still controversial. The aim of our analysis was to asses the role of virtual computed tomography colonography (CTC) in the follow-up of patients who underwent surgery for colorectal cancer (CRC).

Methods: From January 1998 through March 2001, 35 CRC surgical treated patients (all adenocarcinoma, 18 female, 17 male, 14 rectum, 20 colon, 1 r-s junction, grading 2 G1, 23 G2, 3 G3, 7 GX, 8 Dukes A, 14 Dukes B, 13 Dukes C, mean age 63 years, age range 43-78), entered our surveillance program with CTC. Patients were following a schedule which consist in annual conventional colonoscopy, liver US and chest X-ray, physical examination and serum CEA every 3 months for the first 3 years from diagnosis, every 6 since 5th year. Bowel was regularly prepared with standard setting for traditional colonic exam and after air insufflate; multislice spiral CT (Somaton Plus 4 Volume Zoom, Siemens) examination of the abdomen and pelvis was performed. Patients were scanned in supine and prone position using the following parameters: 1 mm collimation, 1 mm reconstruction index, 8 mm/sec table speed, and mAs 80 with the patient in the prone position, and then after the injection of intravenous contrast medium (60 sec delay), with the patient in the supine position, using 120 mAs. Images were evaluated on a dedicated workstation.

Results: We consider as gold standard for virtual exam the conventional colonoscopy and related pathologic exam. Thirty patients were negative for any pathologic aspect. We checked only one false positive. We found: 3 patients with liver metastases confirmed by RMN, 1 patient with 2 basal pulmonary nodules, 5 patients with 6 polyps and 1 local anastomotic relapse.

Conclusions: We think that CTC is feasible and can offer, unlike conventional, the opportunity to have a complete TNM owing to liver scan with I.V. contrast, with low patient discomfort; it can also check extra-colonic findings. Our study is still ongoing to subsequently assess if CTC can be considered as first choice exam in the follow-up of patients surgically treated for CRC.

1099 POSTER

Tomudex + folinic acid + 5-fluorouracil (5FU) and preoperative concomitant radiotherapy for locally advanced rectal cancer(LARC): a phase I study

A. Avallone[1], P. Delrio[2], C. Guida[3], P. Marone[4], R. Casaretti[1], R. Palaia[2], G.B. Rossi[4], B. Morrica[3], V. Parisi[2], G. Comella[1]. [1] *National Cancer Institute, Medical Oncology "A", Naples, Italy;* [2] *National Cancer Institute, Surgical Oncology "C", Naples, Italy;* [3] *National Cancer Institute, Radiotherapy, Naples, Italy;* [4] *National Cancer Institute, Endoscopy Unit, Naples, Italy*

Background and Purpose: Preoperative chemoradiation in rectal cancer (RC) is still investigational: improved resectability rates and sphincter preservation with low toxicity are reported. Prolonged venous infusion (PVI) of 5-FU concomitant with postoperative radiotherapy has shown good results in both local tumor control and survival. Nevertheless PVI 5-FU is cumbersone and expensive. Accurate preoperative evaluation by endoscopic ultrasound (EU) is mandatory for a careful selection of patients.