events included: diarrhea, 20%; neutropenia, 11%; acne-like rash (grade 3 only), 9%. No grade 3/4 infusion-related reactions (IRRs) were reported.
Conclusions: The overall confirmed RR of 27% observed in this heavily pretreated population fully met the expectations for the primary endpoint of this study. LABEL confirmed the activity and safety of cetuximab plus irinotecan seen in previous studies.

3056 POSTER

XPA, XPD, ERCC1 and XPG/ERCC5 single nucleotide polymorphisme (SNPs) in oxaliplatin-treated colorectal cancer (CRC)

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Background: Oxaliplatin damages DNA, leading to apoptosis. XPA, XPD, ERCC1 and XPG/ERCC5 are involved in DNA repair, and polymorphic variant in these genes can influence the efficacy of oxaliplatin. We analysed SNPs in these genes and correlated the results with toxicity, time to progression and overall survival and response to oxaliplatin in advanced CRC.
Methods: 42 CRC patients (pts) recruited between April 2002 and May 2005 were treated with oxaliplatin as first line chemotherapy combined with fluoropyrimidine [Moreno I et al. Ann Oncol 2006; 17(Suppl 6): 75 (P-178)]. Update march 2007. DNA was obtained from peripheral blood cells at baseline, and allelic discrimination assay with ABI Prism 7700 was used to analyze SNPs at XPA 5′utr A/G, XPD Lys751 Gln, ERCC1 Thr/Lys and XPG/ERCC5 C/T
Results: Patients characteristics: 21 males/21 females, median age 66 yr (range, 44−79), PS 0−2. Pts with XPA genotype A/A showed lower emesis toxicity (12%) than those with A/G and G/G (20%) ($p = 0.010$). Pts with XPG C/C shower better objective response (74%), than those with C/T and T/T (35%) ($p = 0.03$). Pts with XPG C/C achieved longer time to progression (15.8 months) than those with C/T and T/T (7.5 moths) ($p = 0.009$). Pts with XPG C/C achieved better median survival (33 moths) than those with C/T and T/T (13.9 months) ($p = 0.000$). Pts with XPG C/C and XPA A/G or G/G achieved better time to progression and median survival (21.8 moths and 43.3 moths, respectively) than those others patients (7.5 months and 15.5 months, respectively) ($p = 0.000$). Cox multivariate analysis showed that gender (male), PS (<2), and genotypes XPG C/C and XPA A/G or G/G, were favourable predictive factors.
Conclusion: XPG C/C may be a predictive marker of response and genetic profile XPG C/C and XPA A/G or G/G may be a predictive marker of time to progression and overall survival in oxaliplatin CRC pts. Studies with a larger number of patients should be carried out to confirm these results.

3057 POSTER

Neoadjuvant chemoradiation for locally advanced rectal cancer. Analysis of clinical outcomes

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Background: During the past few decades, significant progress has been achieved in the management of rectal cancer with the introduction of total mesorectal excision.Preoperative radiotherapy appears more effective in terms of local control and toxicity compared to postoperative therapy. Several recent studies show that 5-FU-based chemotherapy enhances tumour response to radiotherapy and preoperative chemoradiotherapy is being increasingly used for stage II and III disease.
Our prospective cohort study will evaluate the impact of neoadjuvant radiochemotherapy at first on toxicity, surgical morbidity and pCR rate and then the local and distant recurrence rates.
Patients and Methods: From 1998 to 2006, 188 consecutive patients, with a tumour with an average distance from the anal verge of 6.5 cm, were treated with neoadjuvant radiochemotherapy. 89 of them (47.4%) had the tumour localized in lower rectum, 82 (43.6%) in the middle one and 17 (9%) to the upper rectum. All the patients were studied by EUS, MR and CT to establish the clinical stage and so decide the therapeutical strategy. These patients, staged as II and III, were submitted to a “long-course” radiochemotherapy. After 4−6 weeks from the end of the neoadjuvant therapy, all the patients were submitted once again to EUS and MR and then operated on.
Results: 164 patients showed a clinical stage III and 24 a clinical stage II. No major complications related to therapy were observed and all the patients have completed the course of therapy. A complete or partial response was observed in 70.7% of the patients and pCR was found in 13.8%. We observed a significant clinical down-staging ($p < .004$). Surgical procedures (112/188 [60%] laparoscopic) carried out were: 156 AR (83.9%), 24 APR (12.9%) and 4 TEM (2.2%). We observer clinical anastomotic leak in 6.3%. Mean nodal-sampling was 14.9. Concerning yTNM, 26/188 patients (13.8%) were in stage 0, 42/188 (22.3%) in stage I, 66/188 (35.2%) in stage II and 54/188 (28.7%) in stage III. Five-years overall-survival and disease-free-survival were respectively 73% and 60%. Pre-treatment clinical stage had no prognostic significance ($p = 0.9321$). On the contrary, postoperative yTNM was significant ($p = 0.0090$) for yT ($p < 0.001$) and yN ($p < .00024$). Non-responder patients had the worse prognosis (5-years survival 30%). The variable with higher prognostic significance was yN ($p < .0003$), especially if we distinguish N1 by N2 ($p < .00022$). With a mean follow-up of 36 months, local recurrence rate was 5.7%.
Conclusions: Our data showed that neoadjuvant chemotherapy in well tolerated and don’t improve the postoperative complication. The post operative stage play an important independent prognostic role in disease free and overall survival. Future neoadjuvat trials should evaluate, with modern molecular biology techniques, correlation between reresistence markers or other molecular markers to stratify patients besed on molecular markers instead of on biologic tumours response.

3058 POSTER

Administration of reduced glutathione in FOLFOX4 regimen in advanced colorectal cancer: effect on oxaliplatin pharmacokinetics and on Pt-DNA adducts formation

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Background: Neurotoxicity is the most common oxaliplatin (OXA) toxicity in FOLFOX4 regimen for patients with advanced colorectal cancer. Recently, Cascinu et al. (JCO 2002; 20: 3478–3483) provided evidence that reduced glutathione (GSH) reduces the OXA-induced neurotoxicity, but GSH influence on the formation of Pt-DNA adducts still remains unknown. This study evaluated the effect of GSH addition on OXA pharmacokinetics(pk) and on Pt-DNA adducts formation
Materials and Methods: 28 patients were given twelve FOLFOX4 courses and randomized to receive either GSH 1,500 mg/m^2 ornormal saline solution (placebo) before OXA. OXA pk and Pt-DNA adducts formation were evaluated at cycles 5, 9 and 12. Total and ultrafiltered platinum were analyzed by atomic adsorption, Pt-DNA adducts in leukocytes (as model for tumour tissue) by adsorptive stripping voltammetry. Pk analysis were done by non-compartmental analysis, statistical analysis by non-parametric Mann-Whitney test
Results: Median total and ultrafiltered platinum pk parameters were comparable to previously reported ones, only median total AUC_{tot} show statistically significant difference being higher in the placebo arm. On the other side, ultrafiltered platinum pk parameters show no statistically significant differences The formation of Pt-DNA adducts was more pronounced in GSH arm (median value at the end of infusion 4.52 Pt atoms/10^6 nucleotides vs. 4.25 Pt atoms/10^6 nucleotides), though not statistically significant.

	Total Pt			Ultrafiltered Pt		
	GSH-OXA	Placebo-OXA	p	GSH-OXA	Placebo-OXA	p
C_{max} (mg/l)	2.47	2.66	0.855	0.196	0.197	0.882
AUC_{tot} (mg*h/l)	127.5	166.9	0.036	4.49	4.43	0.982
Cl_{tot} (l/h)	1.08	0.97	0.385	31.1	33.2	0.235

Conclusions: The addition of GSH to FOLFOX4 regimen is able to reduce the OXA-induced neurotoxicity, without affecting either the OXA pk behaviour or the formation of Pt-DNA adducts, thus assuring that the well-known clinical efficacy is unmodified.

3059 POSTER

Prospective comparison of laparoscopic vs. open total mesorectal excision (TME) for rectal adenocarcinoma

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Background: The continue advancing of laparoscopic surgery has become possible to extend the mini invasive technique to Total Mesorectal Excision