238 POSTER

Gemcitabine (GEM) as salvage treatment in patients (pts) with advanced colorectal cancer (CRC) progressing after treatment with 5-fluorouracil (FU), irinotecan (Iri) and oxaliplatin (oxa)

C. Aschele[1], S. Lonardi[2], S. Garrè[1], C. Caroti[1], M. D'Amico[1], L.M. Pasetto[2], M. Stefani[2], P. Pronzato[3], L. Gallo[1], S. Monfardini[2].
[1] Ospedali Galliera, Dept. of Medical Oncology, Genova, Italy; [2] Padova University Hospital, Dept. of Medical Oncology, Padova, Italy; [3] Ospedale Sant'Andrea, Dept. of Medical Oncology, La Spezia, Italy

Sequential combinations of FU and either IRI or OXA are currently used as standard first and second line treatment for advanced CRC. Multiple studies are also investigating the concomitant use of the three agents up-front. Progressing patients often have an acceptable PS and continue to require treatment. GEM has shown clinical activity in adenocarcinomas of multiple sites and has a favorable toxicity profile. Since September 2000, 35 pts with progressive advanced CRC (males/females: 24/11; median age 65, range 46-79 yrs; ECOG PS 0/1/2: 7/23/5; median CEA 97, range 1-5780 ng/ml) previously treated with FU, IRI and OXA, were thus accrued in a phase II study of GEM (1000 mg/m2 weekly for 7 consecutive courses and then weekly x 3 q 4 weeks) with abrogation of progression as the main end-point. 20 pts had been treated with a triple combination including FU, IRI and OXA as first line therapy and thus received GEM as second line treatment, while for 15 pts GEM was given as salvage treatment after a median of 2 previous CT lines (range 2-4, median administered FU:25,600 mg, median administered IRI:2,430 mg, median administered OXA:1,300 mg). Metastatic disease was at multiple sites, in the liver only and in the lung only in 26, 6 and 3 cases, respectively. Overall, 56 cycles were delivered (87.7% of the planned weekly administrations). The median number of cycles administered to each patient was 2 (range 1-4) and the median number of weeks of CT was 8 (range 3-22). Only 20 of 322 (6.2%) weeks of GEM were delayed because of toxicity while 24 of 322 (7.4%) weeks were delivered at a reduced dose. Toxicity was mild with only 1 and less than 20% of the pts experiencing grade IV (neutropenia) and grade III (nausea and vomiting, neutropenia and thrombocytopenia) events, respectively. Flu-like syndrome was observed in 8 pts but did not exceed grade I. 4 pts are still completing the first cycle. Response was analysed on all the other registered pts according to the intention-to-treat principle (n=31) and 1 PR, 2 MR, 15 SD and 13 PD were observed. Overall, disease progression was abrogated in 18 of 31 cases, equally distributed in the two subsets of pts (57.8% in the cohort receiving GEM as second line treatment and 58.3% in the group receiving GEM as salvage therapy after two or more previous CT lines).

These data suggest that GEM is well tolerated and may abrogate disease-progression in approximately half of the pts refractory to FU, IRI and OXA. A larger confirmatory trial is planned.

239 POSTER

A phase II trial of oxaliplatin (L-OHP) and UFT/leucovorin (LV) for advanced colorectal cancer (ACC) in elderly patients

G. Rosati[1], S. Cordio[2], G. Blanco[2], R. Bordonaro[2], G. Reggiardo[3], L. Manzione[1]. *[1] "S. Carlo" Hospital, Medical Oncology Unit, Potenza, Italy; [2] "S. Luigi" Hospital, Medical Oncology Unit, Catania, Italy; [3] Medi Service, Data Management Unit, Genova, Italy*

Background: Colorectal cancer is usually diagnosed in elderly patients. Since the increase of life expectancy makes chemotherapy more appealing in this setting, we test the activity and toxicity of L-OHP and UFT/LV in patients with ACC aged 70 or older. Patients and methods: A two-stage trial was planned with an accrual goal of 44 patients. The treatment included L-OHP 65mg/m2 on day 1 and 8 plus UFT 300mg/m2 and LV 90mg in three divided doses given on days 1-14 of each three-week cycle. Patients were followed by a geriatric and a quality of life assessment with specific scales and EORTC-QLQ-C30 questionnaire.

Results: The first 23 patients were evaluable for toxicity and 17 for response, M/F 14/9, age 70 to 89, PS 0/1/2 10/12/1, colon 15 and rectum 8. Metastases locations: liver 17, lung 11, peritoneal carcinomatosis 5. 5/23 had had prior adjuvant chemotherapy and 2 radiotherapy outside on target lesions. Myelosuppression was mild with 5 grade 2 thrombocytopenia and 2 grade 2 anemia. Non-hematological toxicities were grade 3 diarrhea in 3 cases and grade 1-2 nausea/vomiting in 6 patients. Intermittent grade 1-2 neurotoxicity was observed in 4. Only one case of unacceptable cardiotoxicity was registered. Eight (47%) patients had an objective response, complete in 1 and partial in 7 cases.

Conclusions: These preliminay results confirmed that this tested chemotherapy combination is active and tolerated in elderly patients with ACC.

240 POSTER

The potential role of TGF-beta-1, TGF-beta -2 and TGF-beta-3 proteins expression in colorectal carcinomas, and their possible correlation with classic histopathologic factors and patients survival.

A.C. Tsamandas[1], V. Zolota[1], P. Ravazoula[1], T. Kourelis[2], C. Kalogeropoulou[3], I. Tsota[3], T. Petsas[3], K. Tepetes[4], D. Bonikos[1], D. Kardamakis[3]. *[1] University of Patras School of Medicine, Department of Pathology, Patras, Greece; [2] University of Patras School of Medicine, Medical Oncology, Patras, Greece; [3] University of Patras School of Medicine, Radiology, Patras, Greece; [4] University of Patras School of Medicine, Surgery, Patras, Greece*

Background: This study investigates TGFbeta1, TGFbeta2 and TGFbeta3 proteins expression in patients with colorectal carcinoma and evaluates their correlation with classic prognostic markers and patients' survival.

Materials and Methods: The study comprised 124 patients with colorectal carcinoma. According to Astler-Coller system, 42 tumors were of stage A, 42-B, 48-C and 20-D, whereas 106 tumors were low-grade and 18 high-grade of malignancy. On paraffin sections the streptavidin-biotin technique, using antibodies to TGFbeta 1, TGFbeta 2 and TGFbeta 3 (SantaCruz, USA) was employed. Staining results followed morphometric analysis and were correlated with clinicopathologic parameters.

Results: TGF beta1 protein was expressed in 88/124 (71%) carcinomas whereas TGFbeta 2 and TGFbeta 3 proteins were detected in all tumors examined. Normal colonic mucosal epithelial cells expressed less TGFbeta 2 ($p<0.01$ compared to neoplastic cells) and less TGFbeta 3 ($p>0.05$ compared to neoplastic cells), but not at all TGFbeta 1. Statistical analysis revealed higher expression of TGFbeta1 in low grade carcinomas ($p=0.009$) and higher TGFbeta 2 presence in advanced stage tumors ($p=0.008$). TGF-beta1 expression was related with higher disease free survival and higher total survival ($p<0.05$ respectively). TGFbeta2 presence was correlated with worse prognosis ($p<0.05$). Cox analysis revealed that besides tumor grade and stage, TGFbeta 1 expression constituted independent prognostic factor.

Conclusions: This study shows that in cases of colon adenocarcinoma there is different expression of TGFbeta 1, TGFbeta 2 and TGF beta3. TGFbeta 1 may be implicated in the pathogenesis of these tumors since it is expressed only within neoplastic and not normal cells. TGFbeta 1 is related with higher disease free survival, higher total survival and constitutes an independent prognostic factor. In the late stages, TGFbeta 2 seems to be involved in tumor progression and it is related with worse prognosis.

241 POSTER

Phase II study of bi-weekly oxaliplatin,UFT and leucovorin (OXA-UFT-LV) in pretreated metastatic colorectal cancer(MCRC).

E. González-Flores[1], R. Luque[1], J. Valdivia[1], V. Conde[1], A. Irigoyen[1], J.R. Delgado[1], P. Ballesteros[1], A. Bezares[2], E. López[2], J. Belón[1]. *[1] HMQ"Virgen de las Nieves", Medical Oncology, Granada, Spain; [2] HMQ"Virgen de las Nieves", Radiotherapy Oncology, Granada, Spain*

Introduction: OXA has previously demonstrated high efficacy combined with 5FU-LV.The combination of UFT and LV is effective and is associated with limited toxicity in the treatment of MCRC. This phase II clinical study was designed to evaluate the efficacy and toxicity of the combination of OXA-UFT-LV for more than 1ª line treatment of MCRC.

Patients and methods: Between 01/00 and 12/01, 23 patients have been included. Mean age is 57 years(39-69), ECOG 0/1/2 ratio 8/3/2. Every patient has received at least one line of previous chemotherapy with 5FU and/or CPT11. This regimen consisted on: OXA 85 mg/m2 D1 and 14+LV 500 mg/m2 2h infusion D1. Oral administration of UFT 300 mg/m2/d (in 2 doses) D1 to 14 and LV 15 mg q 12h D2 to 14.Cycles are repeated every 28 days until progression or toxicity.

Results:. 20 patients are evaluable for response and 23 for toxicity. Up to the current analysis was observed: G1 neurotoxicity in 6/23 (28%) patients;G2 in 3/23(15%) patients; G3 in 1 (7%) patients. Gastrointestinal toxicity:G3-4 diarrhea1 (7%) patients,G3-4 nausea and vomiting 1 (7%) patients. No dose reductions have been necessary. Efficacy results: 5/20(25%) partial response,7/20(35%) stable disease and 8 progression(40%).