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POSTER

Oxaliplatin or Irinotecan based chemotherapy for metastatic colorectal cancer in the elderly

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Background: Oxaliplatin and irinotecan are widely used in metastatic colorectal carcinoma. Their tolerance and efficacy are unknown in elderly patients (pts) over 75 years.

Methods: All consecutive pts over 74 years treated with oxaliplatin or irinotecan for metastatic colorectal cancer from January 1999 to June 2002 were retrospectively enrolled. Tumour response was assessed with CT examination every 2 to 3 months and toxicity was collected at each cure according to WHO criteria.

Results: Sixty-six pts were enrolled from 12 centres. Median age was 78 years (range: 75-88), 39 pts had no severe co-morbidity according to Charlson score. Forty four and 22 pts received oxaliplatin or irinotecan respectively, in combination with 5-fluorouracil +/- folinic acid or raltitrexed in 64 pts. A total of 545 chemotherapy cycles were administered in first (41%), second (51%) and third (8%) line. Dose reduction occurred more frequently in pts over 79 years (31 vs 48%, p2 (12 vs 44%, p=0.04). No treatment-related death occurred. Chemotherapy improved performance status and weight in 38 and 28% of pts, respectively.

Conclusion: In selected elderly patients, chemotherapy with oxaliplatin or irinotecan is well tolerated with comparable efficacy than in younger patients.

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The carcinoembryonic antigen (CEA) family: gene expression in colorectal tumor samples by real-time quantitative polymerase chain reaction (RT-QPCR)

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Background: The CEA family is composed of 7 proteins (CEACAM1, CEACAM3, CEACAM4, CEACAM5, CEACAM6, CEACAM7 and CEACAM8) which differ according to their C-terminal domain. CEACAM1, CEACAM3 and CEACAM4 have transmembrane and cytoplasmic domains, while CEACAM5, CEACAM6, CEACAM7 and CEACAM8 are attached to the cell membrane via glycosyl phosphatidyl inositol. Immunohistochemistry and in situ hybridization have shown that CEACAM1, CEACAM5, CEACAM6 and CEACAM7 are expressed in normal tissue and in colorectal carcinoma, while CEACAM3, CEACAM4 and CEACAM8 are not expressed in epithelial tumors. To date, there is no clear correlation between the CEA family and clinicopathological factors. We assessed mRNA expression of CEA in normal tissue and in colorectal tumor samples by RT-QPCR and correlated results with clinicopathological characteristics.

Patients and Methods: mRNA was isolated from 16 surgery colorectal tumor samples and transformed into cDNA with RT-PCR. With probes marked for gene expression, mRNA expression was quantified (ABI Primers 7700) for CEACAM1, CEACAM3, CEACAM4, CEACAM5, CEACAM6, CEACAM7 and CEACAM8.

Results: The mRNA expression levels of CEA in tumor were different from levels in normal tissue: CEACAM1 (37.5%), CEACAM3 (31%), CEACAM4 (44%), CEACAM5 (63%), CEACAM6 (87%), CEACAM7 (37%) y CEACAM8 (44%). CEACAM3, CEACAM4 and CEACAM8 mRNA expression, which was not detected by immunohistochemistry, was observed in normal tissue.

CEACAM 5 was expressed in 5 of 7 (71%) stage II patients (pts), 2 of 3 (67%) stage III pts and 4 of 6 (67%) stage IV pts. CEACAM6 was detected in 7 of 7 (100%) stage II pts, 1 of 3 (33%) stage III pts, and 5 of 5 (100%) stage IV pts. CEACAM8 was detected in 6 of 7 (86%) stage II pts and 1 of 5 (17%) stage IV pts.

Conclusions: These preliminary data show that RT-QPCR is a sensitive method for CEACAM analysis. CEACAM5 and CEACAM6 are overexpressed in tumors and CEACAM7 is downregulated. The clinical signif-

icance of CEA family detection in surgery tumor samples by RT-QPCR needs further evaluation.

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The impact of microsatellite instability and its correlation with p53 expression in sporadic colorectal cancer (sCRC)

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Background: Inactivation of one of the mismatch repair (MMR) genes leads to microsatellite instability (MSI) implicated in the pathogenesis of 15-20% of sCRCs (mutator pathway). These cases constitute a particular group of sCRCs with distinct clinicopathological characteristics, different response to chemotherapy and better prognosis. On the contrary, p53 is implicated in loss of heterozygosity pathway (LOH) which leads to microsatellite stable carcinomas. Overexpression of p53 is usually correlated with worse prognosis.

We studied MSI via the expression of MLH1, MSH2-1 and MSH2-2 proteins and correlated them with p53 expression and other clinicopathological parameters.

Patients and Methods. 88 patients (pts) with sCRCs and a 5 to 10 year follow-up (M/F 51/35, mean age 61.4/60, 14 of them less than 50 years old) were included. The tumors, 26 of the right and 60 of the left colon, were staged according to Dukes classification as: 14 stage A, 29 B, and 43 stage C. Paraffin sections of tumor and adjacent normal mucosa were immunohistochemically studied for MSI, using monoclonal antibodies against MSH2-1, MSH2-2 and MLH1 proteins. Tumors with loss of at least one gene protein expression of were defined as MMR-. Expression of p53 was evaluated as the percentage of positive nuclei via an interactive morphometric image analysis program.

Results. Loss of at least one MMR protein expression was verified in 20 (22.2%) of sCRCs; MSH2-1 in 15/86 (17.4%), MSH2-2 in 10/86 (11.6%) and MLH1 in 5/86 (5.8%) of pts. The MMR-/MMR+ mean age of pts was 57.4/63.0 (p=0.055). MMR- pts were characterized by right-sided (p<0.0001), mucinous (p<0.08), partly mucinous (p<0.05) or low differentiated carcinomas (p<0.005). Survival rates were better for MMR- pts. High expression of p53 was observed in MMR+ cases and correlated with worse survival (p<0.005). We noted minimal to nil percentage of p53 expression in MSH2-1 (p<0.001), MLH1 (p<0.05) and MMR- (p<0.0001). No statistically significant difference was observed for MSH2-2- carcinomas. In multivariate analysis stage, p53 and MLH1 protein expression were shown to be independent prognostic factors.

Conclusions. MMR- sCRCs show distinct clinicopathological characteristics, better prognosis and absence or near absence of p53 expression. MLH1 expression seems to be an independent prognostic factor. p53 overexpression in MMR+ cases correlates with worse prognosis.

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Prognostic factors of survival after oxaliplatin therapy in colorectal cancer patients pretreated by irinotecan

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Background: Oxaliplatin (OHP) is effective as first and second line agent in metastatic colorectal cancer (CRC). The activities of OHP and irinotecan (CPT) alone or in combination with 5-fluorouracil (5FU) are comparable, but the data on the effectiveness of OHP in patients pretreated by CPT are limited.

Patients and Methods: The survival of 77 patients with metastatic or inoperable loco-regionally recurrent CRC treated with OHP after previous CPT therapy was analyzed retrospectively. 62 patients (81%) had liver metastases. 55 patients were treated by combination of OHP with 5FU, 25 patients were treated by OHP combined with raltitrexed (TOMOX), and 3 patients received sequentially OHP with 5FU and TOMOX. The impact of clinical and biological parameters on survival was analyzed by log-rank test. Multivariate analysis was performed by Cox regression method, and the results were expressed as hazard ratio (HR).

Results: The median survival of all patients was 10.6 months (1 year survival 43%). The median survival from the diagnosis of advanced/metastatic CRC was 34.3 months. On univariate analysis, the survival was not significantly affected by the line of the treatment, presence of lung metastases,