

mRNA and protein levels show important and specific elevations. Moreover, in papillary carcinoma the increase of α (1,6)FT content has been related with the biological aggressiveness and anaplastic transformation of the primary tumour. In previous studies we have demonstrated a significant increase of α (1,6)FT immunohistochemical expression in colorectal cancer (CRC) tissues. This enzyme expression was also higher in advanced stages of the tumour than in early ones. In the present study, we have evaluated the relation between α (1,6)FT expression and the patient survival with the aim to determinate the prognostic value of α (1,6)FT expression in CRC.

With this purpose, 101 colorectal tumour tissues were analysed by immunohistochemistry. The semiquantitative staining analysis was performed by expert pathologists. The statistical analysis was performed by the Kaplan-Meier method, the log-rank test and the Cox's multivariate analysis. The difference between the overall survival and the disease-free survival rates from patients with weak (82.6% and 79.7%, respectively) and strong (79.4% and 69.3%, respectively) α (1,6)FT expression was not statistically significant ($p = 0.61$ and $p = 0.22$, respectively). Nevertheless, we found that patients with weak α (1,6)FT expression present relapse-free survival rates (94.9%) significantly higher ($p = 0.012$) than patients with strong expression (77.8%). Besides, the strong α (1,6)FT expression in patients with advanced stages and lymph node invasion was associated with a worse rate of overall and disease-free survival. On the other hand, in multivariate analysis the lymph node metastasis was found to be an independent prognostic factor for disease-free survival ($p = 0.004$), as well as the intensity of α (1,6)FT expression was the only prognostic factor for relapse-free survival ($p = 0.014$).

In summary, it seems that α (1,6)FT immunohistochemical expression is really associated with the capacity of the primary tumour to form new tumour focus in the intestinal wall. Thus, α (1,6)FT expression could be a clinically useful information for patient survival.

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POSTER

Impact of the number of examined lymph nodes on prognosis in colon cancer: a population based study in North Netherlands

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Background: Lymph node metastasis is a determinant factor in the adjuvant treatment and an important predictor of survival in colon cancer patients. Adequate surgical resection and punctual pathological examination of the resected specimen is desirable. We studied whether the number of reported lymph nodes examined in colon specimens has an effect on stage migration and survival.

Patients and Methods: Between 1998 and 2002 a total of 2751 resections of colon cancer were performed in 17 hospitals and analyzed in 7 pathology laboratories in the northern part of The Netherlands. The Comprehensive Cancer Centre North-Netherlands, which covers a population of 2.1 million inhabitants, superintends the quality of guidelines and follow-up of cancer patients. Factors associated with the number of examined lymph nodes were studied as well as the effect of tumor characteristics and number of lymph nodes on nodal status and survival. The influence of possible determinants was tested in a general linear model after transformation for continuous variables and binary logistic regression analysis for nominal variables. Survival was calculated from the date of diagnosis until the date of death, the date of most recent linkage with the municipal population registries or the date of last contact.

Results: The number of harvested and examined nodes increased with higher T-stage ($p < 0.001$) and a mucinous morphology ($p = 0.002$), but decreased with increasing age ($p < 0.001$). Localization was also of influence on the number of examined nodes. The proportion of node-positive patients increased with a larger number of nodes examined. T-stage and the number of examined nodes were of significant influence on nodal status. Based on co-morbidity and age, adjuvant chemotherapy was given to 52% of node-positive patients. The 5-year overall survival rate was 49.6% for node-positive patients versus 67.8% for node-negative patients. Survival increased with more nodes examined in node positive as well as node negative patients.

Conclusions: In this study T-stage, localization and patient age are of significant importance for the number of nodes examined by the pathologist. A higher number of examined nodes was associated with an increase in node-positivity and an improved accuracy of the pathological status. Conscientious pathological sampling with more harvested nodes seems to improve nodal staging and through this, more patients can be offered adjuvant treatment leading to a better survival.

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POSTER

Anti-tumour effect of L-arginine on gastric and colorectal cancers

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Background: L-arginine has been shown to have anti-atherogenic, anti-oxidant and immunomodulatory actions. The effect of L-arginine on gastrointestinal tumours has not been studied. This study aimed to evaluate the effect of L-Arginine on gastric and colorectal cancer cell lines in terms of effects on cell growth and the cell cycle.

Materials and Methods: AGS (gastric adenocarcinoma) and WiDr (colorectal adenocarcinoma) were used. L-arginine was added at various concentrations and time points. Cell proliferation was assessed using MTT assay. Flow cytometry was undertaken to analyse effects on the cell cycle. Three experiments were performed with six replicates undertaken for the MTT assay. Statistical analyses were undertaken using the Student t test.

Results: There was inhibition of growth in both AGS and WiDr cells in a dose-dependent manner. Growth inhibition was 22.7% ($p < 0.01$) for AGS cells and 32.5% ($p < 0.05$) for WiDr cells when incubated with 8 mM L-arginine after 48 hours compared with untreated cells. When incubated with 32mM L-arginine the inhibition was 61.5% ($p < 0.01$) for AGS cells. With WiDr cells the inhibition was 60.8% ($p < 0.01$) at 32 mM L-arginine. Flow cytometric analysis of the cell cycle did not show any differences between L-arginine-supplemented and non-supplemented AGS and WiDr cells.

Conclusion: L-Arginine inhibits cell growth of gastric and colorectal cancer cells in a dose-dependent manner. These results suggest that alteration of cell cycle kinetics is not the mechanism of this inhibition and further studies are required to understand how this inhibition occurs.

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POSTER

Capecitabine or Folinic acid/Fluorouracil i.v. bolus plus Eloxatin evaluation (COFFE trial) in metastatic colorectal carcinoma (MCR): final results of the Southern Italy Cooperative Oncology Group (SICOG) phase III trial 0401

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Background: Preliminary safety analysis of the biweekly OXXEL regimen compared with the biweekly OXAFUFU regimen has previously been reported. Here we report on the response rate (RR), which was the primary end-point of this phase III trial.

Methods: Patients (pts) with MCR, previously untreated for their metastatic disease, and with at least one bidimensionally measurable lesion, were randomized, after stratification for performance status (0 vs 1-2), and previous adjuvant treatment (yes vs not), to receive either OXAFUFU: oxaliplatin 85 mg/sqm iv on day (D) 1, levo-folinic acid 250 mg/sqm plus 5-fluorouracil 850 mg/sqm iv bolus on D 2; or OXXEL: oxaliplatin 100 mg/sqm iv on D 1, capecitabine 1,000 mg/sqm twice daily orally from D 1 (evening) to D 11 (morning). Cycles were delivered q 2 weeks up to progressive disease (PD), or for a maximum of 12 cycles. A total of 242 pts and 257 PDs have an 80% power to demonstrate, with an alpha error = 0.05, a 15% difference in RR (30% vs 45%), and a 50% prolongation of progression-free survival (PFS). Response and toxicity were assessed according to WHO criteria.

Results: From May 2004 to Jan. 2007, 306 (OXAFUFU, 156; OXXEL, 150) eligible pts were recruited from 23 SICOG centers. Characteristics (OXAFUFU vs OXXEL arm) were: males, 54% vs 66% ($P = 0.029$); median age (range), 65 (37-83) vs 64 (39-84) yrs; age ≥ 70 yrs, 42% vs 32% ($P = 0.062$); primary colon, 70% vs 72%; adjuvant CT, 24% vs 23%; PS 0, 59% vs 61%; liver mets, 76% vs 84%; ≥ 2 sites, 57% vs 49%; basal CEA ≥ 5 ng/mL: 78% vs 77%. Median number of delivered cycles was 8 (range, 2-12) in both arms. CRs+PRs were 6+45, RR=33% (95% CI, 0.25-0.41) in the OXAFUFU arm, and 11+39, RR=33% (95% CI, 0.26-0.42) in the OXXEL arm. So far, a PD was registered in 211 pts; median PFS was 6.4 (95% CI, 5.8-7.0) mo. for OXXEL arm, and 6.1 (95% CI, 5.5-6.7) mo. for OXAFUFU arm (HR = 0.92; 95% CI, 0.70-1.21, $P = 0.550$). Severe neutropenia (12% vs 27%) and febrile neutropenia (6% vs 13%) favored the OXXEL regimen, but $G \geq 3$ emesis (7% vs 2%), diarrhea (14% vs 8%), and skin toxicity (4% vs <1%) were less frequent with the OXAFUFU regimen.