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.

3042 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.

3043 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.

3044 POSTER

Capecitabine or Folinic acid/Fluorouracil i.v. bolus plus Eloxatin evaluation (COFFE trial) in metastatic colorectal carcinoma (MCRC): 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 OXAFAFU 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 MCRC, 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 OXAFAFU: 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 (OXAFAFU, 156; OXXEL, 150) eligible pts were recruited from 23 SICOG centers. Characteristics (OXAFAFU vs OXXEL arm) were: males, 54% vs 66% ($P = 0.029$); median age (range), 65 (37−83) vs 64 (39−84) yrs; age $\geqslant$70 yrs, 42% vs 32% ($P = 0.062$); primary colon, 70% vs 72%; adjuvant CT, 24% vs 23%; PS 0, 59% vs 61%; liver mets, 76% vs 84%; $\geqslant$2 sites, 57% vs 49%; basal CEA $\geqslant$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 OXAFAFU 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 OXAFAFU 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 $\geqslant$ 3 emesis (7% vs 2%), diarrhea (14% vs 8%), and skin toxicity (4% vs <1%) were less frequent with the OXAFAFU regimen.

Conclusions: Within the limits of the current results, the OXXEL regimen was equivalent to the OXAFAFU regimen in terms of efficacy. Comparative analysis of quality of life of pts in the two arms of treatment is ongoing.

3045 POSTER

Serious arterial thromboembolic events (sATE) in patients (pts) with metastatic colorectal cancer (mCRC) treated with bevacizumab (BV): results from the BRiTE registry

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Introduction: Bevacizumab (BV, Avastin®) prolongs overall survival (OS) and progression-free survival (PFS) when added to 1st-or 2nd-line chemotherapy (CT) in mCRC. Though serious toxicities specific to BV are uncommon, a retrospective pooled analysis of 5 randomized trials showed an association of arterial thromboembolic events (ATEs) with BV use (3.8% vs 1.7% with CT alone), with age ⩾65yr and prior history of ATE identified as associated risk factors (Skillings, JCO, 2005). The BRiTE mCRC registry evaluated BV-associated serious adverse events (SAEs), including ATEs presenting as SAEs (sATE), in a general practice setting.
Methods: Patients and methods have been described (Hedrick, ASCO, 2006;A3536). History of sATE, timing of prior sATE relative to starting BV, and use of anti-platelet (anti-plt) therapy were summarized. Definition of sATE included myocardial infarction (MI), cerebral vascular accident (CVA), transient ischemic attack (TIA), and peripheral arterial disease. Incidence rate of sATE was expressed as events per patient-year of follow-up. Fisher's exact test and multiple logistic regression were used to assess the univariate and multivariate associations.
Results: Median follow-up time was 19.6 months. Of 1953 evaluable patients, 45.9% (n = 896) were ⩾65yr, 18.0% (n = 352) had history of sATE, and 11.2% (n = 219) received anti-plt therapy. A total of 38 sATE [CVA (n = 14), MI (n = 11), sudden cardiac death (n = 1), TIA (n = 7), and other (n = 5)] were reported in 34 (1.7%) patients. Median time to sATE was 3.6 months. The calculated sATE rate was 2.2/100 patient-years overall and 4.7/100 patient-years in patients with prior sATE. Table 1 summarizes the results of univariate and multivariate analyses.
Conclusions: In this uncontrolled observational study of BV-treated mCRC patients, the incidence of sATEs associated with BV use was comparable to the rate of analogous events reported in previous controlled trials of BV in mCRC. In this multivariate analysis, a prior history of sATE and ECOG PS were found to be associated with an increased risk of developing an sATE while on BV therapy.

Table 1.

Characteristics	Univariate sATE frequency	Multivariate P value
ECOG PS		
0	7 (0.8%)	0.020
⩾1	23 (2.4%)	
ATE history		
Yes	13 (3.7%)	0.018
No	21 (1.3%)	
Hypertension history		
Yes	21 (2.5%)	NS
No	13 (1.2%)	
Age ⩾65yr		
Yes	20 (2.2%)	NS
No	14 (1.3%)	
Age ⩾65yr		
With ATE history	11 (4.3%)	NS
Without ATE history	9 (1.4%)	

NS = not significant.

3046 POSTER

A randomized, open-label phase II study evaluating the efficacy and safety of FOLFOX6 + Cetuximab versus FOLFIRI + Cetuximab as first-line therapy in patients with metastatic colorectal cancer

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Background: FOLFOX6 and FOLFIRI are standard regimens in first-line mCRC. The IgG1 monoclonal antibody cetuximab (Erbitux ®) has proven activity in combination with chemotherapy. This trial aimed to compare cetuximab plus FOLFOX6 (Arm A) with cetuximab plus FOLFIRI (Arm B) as first-line therapy in mCRC pts.
Material and Methods: Pts were randomized to receive either: FOLFOX6 (folinic acid [FA] 400 mg/m^2 administered with oxaliplatin 100 mg/m^2, followed by 5-FU 400 mg/m^2 bolus, then 5-FU 2400 mg/m^2 over 46 hours) or FOLFIRI (same 5-FU/FA with irinotecan 180 mg/m^2) every two weeks. Both arms received cetuximab, 400 mg/m^2 initial dose, then 250 mg/m^2 /week. The primary endpoint was the progression free survival (PFS) rate at 9 months, with secondary endpoints of 3-, 6-, 12-month PFS rates, objective response rate (RR), overall survival (OS) and toxicity.
Results: Between July 2005 and July 2006, 155 pts at 25 centers in 13 countries were randomly assigned to arm A (n = 77) or Arm B (n = 78). In total, 150 patients received study treatment (Arm A: n = 76, Arm B: n = 74).

Characteristics	Arm A (n = 76)	Arm B (n = 74)
Median age (years)	62	63
ECOG Performance Score		
0	46 (61%)	38 (51%)
1	30 (39%)	36 (49%)
Gender		
Female	34 (45%)	29 (39%)
Male	42 (55%)	45 (61%)
Prior therapy		
Neoadjuvant	4 (5%)	3 (4%)
Adjuvant	12 (16%)	9 (12%)
None	60 (79%)	62 (84%)
Metastases at initial diagnosis[a]	44 (59%)	46 (62%)
Number of involved organs		
1−2	58 (76%)	56 (76%)
>2	18 (24%)	18 (24%)

[a]Missing information in one patient of arm A.

Conclusions: No significant differences in pt characteristics occurred between the two treatment arms. Final data (PFS-rates, RR, OS, toxicity) will be presented within the meeting.