T4 tumours and T1-4N2 tumours. Patients received 12 weeks of neoadjuvant capecitabine (2000mg/m2/day po for 14 days every 3 weeks) and oxaliplatin (130mg/m2 iv every 3 weeks). Starting on week 13, capecitabine was continued at 1650mg/m2/day continuously with concomitant radiotherapy 45Gy in 25 fractions followed by 5.4-9 Gy boost to primary tumour. TME was planned 6 weeks after chemoradiation. Post-operatively, patients received 12 weeks of capecitabine at 2500mg/m2/day for 14 days every 3 weeks. MRI was repeated after chemotherapy and CRT.

Results: Between November 01 and November 02, 22 patients were recruited. Median age was 62 (range=38-80). 21 patients had tumour threatening CRM. 19 patients were evaluable for radiological response and 18 patients have proceeded to TME. Following neoadjuvant capecitabine/oxaliplatin, all patients had objective responses (1 CR, 18 PRs). In addition, 80% of patients had symptomatic responses in a median of 22 days (i.e. after one cycle of chemotherapy) including reduced rectal bleeding (100%), improvement in diarrhoea/constipation (79%), diminished pelvic pain/tenesmus (64%) and weight gain/stabilisation (100%). Following CRT, tumour response was sustained in all patients. One patient was still inoperable, but all other patients had R0 resection with tumour regression away from the CRM. Pathological CR was found in 5 patients (28%) and in an additional 8 patients (44%), only microscopic tumour foci were found on surgical specimens. One patient died from myocardial infarction and 1 from pulmonary embolism. No grade 4 toxicity occurred during chemotherapy or CRT.

Conclusion: Capecitabine and oxaliplatin prior to synchronous CRT and TME produces almost universal tumour regression, rapid symptomatic response and may facilitate the achievement of R0 resection.

306 POSTER

Optimox study: Folfox7 compared to Folfox4 in metastatic colorectal cancer (CRC). Results of a randomized study.

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Background: FOLFOX4 has shown superiority over LV5FU2 in first-line therapy of metastatic CRC (de Gramont; J Clin Oncol 18:2938-2947, 2000). The limiting toxicity of the FOLFOX4 regimen is a cumulative sensory neurotoxicity which imposes to stop therapy in patients still responding. In the OPTIMOX study, a limited number of cycles (6 cycles of FOLFOX7) was administered to decrease the neurotoxicity and to later allow FOLFOX reintroduction.

Materials and methods: Patients (pts) were randomised between (arm A) FOLFOX4: oxaliplatin 85 mg/m^2 day (d)1, and folinic acid, 200 mg/m^2 d1 and d2, 5FU bolus 400 mg/m^2, followed by 5FU 22h continuous infusion 600 mg/m^2 d1 and d2 every two weeks and (arm B) FOLFOX7: oxaliplatin 130 mg/m^2 day (d)1, and folinic acid, 400 mg/m^2 d1 only, followed by 5FU 46h continuous infusion 2400 mg/m^2 every two weeks for 6 cycles followed by sLV5FU2: folinic acid, 400 mg/m^2 d1, 5FU bolus 400 mg/m^2, followed by 5FU 46h continuous infusion 2400-3000 mg/m^2 every two weeks for 12 cycles. FOLFOX7 was then reintroduced for 6 cycles or earlier in case of progression on sLV5FU2 in patients having a response or stable disease at the first FOLFOX administration. 623 pts have been enrolled. Arm A, 312 pts (%): M/F=59/41, PS 0/1/2=52/39/8, median age=63[29-80]; Arm B, 313 pts (%): M/F=61/39, PS 0/1/2=53/38/9, median age=64[32-80].

Results: Grade 3-4 toxicity (% of pts) was in arm A (FOLFOX4)/arm B (FOLFOX7): neutrophils 26/20, platelets 3/11, nausea 4/7, mucositis 2/4, diarrhea 9/9, hand-foot 0/2, alopecia 0/4, neurotoxicity 13/13, fatigue 1/1. Response rate (409 evaluated pts) was 58% in arm A (FOLFOX4) and 64% in arm B (FOLFOX7). Progression at first evaluation was 9% in arm A and 7% in arm B. The primary endpoint is the time to disease control (TDC) which is the progression-free survival of FOLFOX4 or FOLFOX7-sLV5FU2 plus the progression-free survival (PFS) of FOLFOX reintroduction in case of second response or stabilization. Median TDC was 10.3 months in arm A and 12.3 in arm B.

Conclusions: FOLFOX7 followed by sLV5FU2 has similar toxicity and efficacy than FOLFOX4 and is a more convenient regimen. Updated data for the whole population should be available for the meeting concerning Response Rate, PFS, TDC, % of surgery of metastasis and FOLFOX7 reintroduction.

Central nervous system tumours

307 POSTER

Upregulation of HC gp-39 gene in astrocytic gliomas

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Background: Astrocytic gliomas are highly malignant, lethal and the most common glial tumors of the central nervous system. Present knowledge recognizes only a fraction of the biological mechanisms presumably to initiate and promote astrocytic glioma formation. Changes in gene expression are important determinants of normal cellular physiology and, if disturbed, directly contribute to abnormal cellular physiology, including cancer. In this context, the identification, cloning and characterization of differentially expressed genes can be expected to provide relevant and important insights into the molecular determinants of tumor initiation and progression.

Materials and Methods: Serial Analysis of Gene Expression (SAGE) has been used for the comparison of gene expression profiles between normal brain and glioblastoma multiforme (GBM). Expression levels of about 47000 genes represented by approximately 284000 of 10 bp "tags" in normal brain and GBM SAGE libraries were compared by accessing SAGEmap database of NCBI. Northern blot hybridization was used for verification of SAGE results.

Results: SAGE showed that human cartilage glycoprotein-39 gene (HC gp-39) had the greatest change in tumour cells. The abundance of HC gp-39 tags was 82 fold higher in GBM library. Northern analysis of brain tumour and normal brain tissue panels confirmed the results of SAGE and showed very high expression levels of HC gp-39 gene found exclusively in astrocytomas of higher grades, anaplastic astrocytoma and GBM. Overexpression of this gene was detected in 14 of 16 GBMs and 6 of 16 anaplastic astrocytomas analyzed. Two GBM samples revealed lower content of HC gp-39 mRNA as compared to other 14 GBM samples but still higher than in normal brain. Low level of HC gp-39 mRNA was detected in samples of normal brain adjacent to anaplastic astrocytomas and GBMs, this mRNA was not detectable at all in WHO grade II astrocytomas and in adjacent normal brain samples. It was not also detected in other brain tumour types. In addition to 1.7 kb mRNA present in all positive cases and found in human chondrocytes and synoviocytes, Northern blot hybridization revealed the larger-sized transcript of HC gp-39. This larger-sized transcript was associated mostly with astrocytomas of higher grades and could arise from alternative processing that may alter the translation product or regulate mRNA stability.

Conclusion: The overexpression of HC gp-39 gene and the appearance of larger-sized transcript may be an important feature of higher grades astrocytomas and can be used as an additional factor for distinguishing between astrocytomas and anaplastic astrocytoma or between GBM and other types of human brain tumours in the cases of ambiguous histological diagnosis.

308 POSTER

Inverse planned stereotactic intensity modulated radiation therapy (IMRT) in the treatment of complex shaped benign meningiomas of the skull base: Acute-, late toxicity and preliminary results.

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Purpose/Objective: The efficiency of radiotherapy for the primary treatment of benign meningiomas and as adjuvant treatment for subtotally resected or recurrent meningiomas has been demonstrated by large modern series. But by using conventional radiotherapy and even stereotactic radiotherapy it is difficult to achieve doses of more than 54 Gy which allows excellent long time control rates, without exceeding the tolerance doses of the surrounding critical normal structures. The aim of this clinical phase I study is to establish inverse treatment planning and IMRT for complex shaped meningiomas of the skull base in the daily clinical routine. Further objectives of this study were to assess the safety, the efficiency and the side effects of inverse planned stereotactic IMRT in the treatment of benign meningiomas of the base of skull.