uptake parameters were provided from the raw data as peak intensity (PI), slope (S), area under curve (AUC), mean transit time (MTT). Volume and contrast uptake changes were compared between the complete (CR) and partial responders (PR) (Kruskal-Wallis test, $p < 0.05$). The response was evaluated from the clinical follow up at 3 months.
Results: At date 55 patients were included and 212 DCE-US were performed. The 3 months follow-up is available for 50 patients and preliminary results are available for 35. The global response rate was 85.7% (30/35): 42.8% (15/35) CR and PR, 11.4% (4/35) stable disease, and 2.8% (1/35) non responder. Volume changes at D+1, D+7 did not predict the CR or PR response. Conversely PI and AUC parameters were significantly higher in CR at D-1 and the ratio values of PI and AUC at D+1 and D+7 /D-1 were significantly lower in CR.
Conclusion: Our preliminary results showed that the use of the raw data in US functional imaging should provide acute parameters of perfusion for early prediction (at D+1 and D+7 after treatment) of tumoral response.

7016 POSTER

Ki67 (MIB1) in differential diagnosis between naevi and melanomas

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Background: Differentiation between naevi and melanomas sometimes may be difficult on routine histological examination. Ki67 (MIB1) immuno-labeling may be useful in this difficult cases.
Materials and Methods: To evaluate Ki67 labeling 65 patients with primary fast growing melanocytic lesions were selected. 20 from Cancer Research Center (Moscow) and 45 were consultative cases. 46 females (71%), 19 males (29%). Of which 13 patients were children under 14 years (20%). Age from 1y. 10 m. to 90 years. Mean age was 36 years. Skin tumors located on trunk in 31 cases (48%), upper and lower extremity in 28 cases (43%), head and neck region in 6 cases (9%). After routine histological examination the primary diagnosis were as follows: naevus with suspicion to melanoma, dysplastic naevus, cellular blue naevus, spindle cell naevus, Spitz naevus, malignant melanoma. All specimens were studied immunohistochemically. We used monoclonal antibody to Ki67 (clone MIB-1, DakoCytomation, USA). Polymer-based detection system with DAB as chromogene was used for immunostaining. In cases with hyperpigmentation we performed Giemse staining for 5 min to avoid misinterpretation of immunostaining. The usage of AEC instead of DAB gave similar results.
Results: In benigh melanocytic skin lesions Ki67 labeling was 5−9%. In melanomas Ki67 labeling was more than 10%. After immunohistochemical analysis diagnosis “naevi” was in 40 cases (62%), melanoma in 25 (38%). Benign lesions were observed in 26 females (65%), 14 males (35%). All 13 children had benign tumors. Melanomas localized on skin of trunk in 12 cases (48%), extremities in 10 cases (40%), head and neck region in 3 cases (12%).
Conclusions: Ki67 (MIB1) labeling can be used to differentiate benign and malignant melanocytic skin lesions. Especially in difficult cases on routine histological examination.

7017 POSTER

Timing of lymph node involvement is an important prognostic factor in stage III patients with thick (>4.0 mm) lower extremity melanoma

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Background: The prognosis of stage III melanoma patients is very heterogenic, therefore the new TNM system was verified in the prospective material. Who has a real chance for cure in this subgroup of patients?
Materials and Methods: Between 249 melanoma patients who had selective ilio-inguinal lymphadenectomy 185 patients with thick (>4.00 mm) melanoma with full information were analyzed. The average depth of invasion was 5.85 mm, tumor was ulcerated in 67 of all cases (36.2%) and Clark V was assessed in 82 patients (44.3%). The median interval between primary excision and the time of lymphadenectomy was 11.1 months.
Results: In 150 of 185 patients recurrent disease were reported, including skin (29pts, 15.7%), lymph nodes (25pts, 13.5%) and distant metastases (53pts, 28.7%) as a first site of recurrence. Others (43pts, 23.2%) had multifocal recurrences and 35 pts (18.9%) were disease free. Skip metastases (positive iliac and negative inguinal) were found in 26 patients (14%). In multivariate Cox analysis only the time between first surgery and lymphadenectomy and the number of involved nodes were significant. Relative risk of death was 5.2 times higher for subgroups which had simultaneously lymphadenectomy (compared to lymph dissection performed more than 1 year after primary excision), and circa 2.7 times higher for more advanced N subgroups (pN3v pN1).
Conclusions: The long time before development of lymph node metastases and before node dissection is a favorable prognostic factor independent of other well known parameters. The value of too early lymphadenectomy (including sentinel node procedure) in this group should be reanalyzed very carefully.

7018 POSTER

Evaluation of serum IL-6, DHEA and DHEAS levels in comparison with two conventional metastatic markers in melanoma

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Based on our previous studies 5-S-cysteinyldopa (5-SCD) a precursor of pheomelanin and S-100 beta (S-100B), an acidic, low molecular weight calcium-binding protein proved to be metastatic markers in melanoma. Interleukin-6 (IL-6) is a multifunctional inflammatory cytokine secreted by malignant cells appeared to be involved in the progression of the disease. Dehydroepiandrosterone (DHEA) and its sulfate (DHEAS) are adrenal hormones with immunostimulating effects. According to the recent reports skin produces DHEA and DHEAS due to the presence of their key enzymes. Data revealed that DHEA, as well as DHEAS had a direct effect on the suppression of IL-6 production, while the circulating DHEAS level has been shown to be correlated negatively with serum IL-6. Our study involved 247 patients (man:127, woman:120) with ($n = 107$) or without ($n = 140$) metastasis of Stage I-IV following surgical intervention. The objectives were to establish the clinical significance of serum levels of IL-6, DHEA and DHEAS measured simultaneously with the melanoma metastasis markers 5-SCD and S-100B. The absence or presence of metastasis was verified by conventional imaging techniques (abdominal UH, X-ray, MR, CT, etc.).
Serum 5-SCD concentration was determined by HPLC with electrochemical detection. IL-6, DHEA, DHEAS and S-100B levels were measured using RIA/IRMA and ILMA methods.
MedCalc Software statistical analysis (Mann Whitney Test, Receiver Operating Characteristic “ROC” curve, logistic regression and multiple regression analysis) was used. Significant increase in the serum concentrations of 5-SCD, S-100B and IL-6 were found in patients with metastasis compared to metastasis-free cases, while a significant decrease in DHEA and DHEAS levels was detected. A significant positive correlation between 5-SCD and S-100B ($P < 0.0001$), 5-SCD and IL-6 ($P < 0.0001$) as well as S-100 and IL-6 ($P < 0.0001$) were found, respectively. In the contrary, a significant negative correlation between IL-6 and DHEAS ($P < 0.0001$) was observed. In order to study the relation of parameters to the localization of metastasis, survival and the progression of the disease further investigations are needed. These results suggest that simultaneous determination of IL-6, DHEA and DHEAS together with 5-SCD and S-100B measured in melanoma patients could be predictive factors of the progression.
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7019 POSTER

Long-term outcome of patients with advanced melanoma

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Background: Advanced melanoma is a devastating disease with a very poor prognosis, an extremely rare long-term survival and limited treatment options. The aim of this study was to evaluate long-term survival and treatment outcomes in a retrospective review of patients with stage IV melanoma.
Methods: Between 1987 and 2006, 452 patients with cutaneous melanoma were followed at our institute. Survival estimates were calculated using the Kaplan-Meier method and multiple logistic regression analysis was performed to assess correlations.
Results: One hundred eighty-eight patients (41.6%) developed distant metastasis. There were 109 males and 79 females, with average age of 54 years at diagnosis. The median survival time was 9 months. Thirty-two patients underwent surgical resection of distant tumor, alone or in combination with other treatments, with a median survival time significantly superior compared with patients not surgically treated ($p < 0.0001$, $HR = 0.3333$, 95% CI : 0.2822–0.5840). The metastatic lesions resected were in the brain (28%), in the gastrointestinal tract (19%), in the lung

(19%), in the skin (16%), in the liver (6%), in the tonsil (6%), in the breast (3%) and in the adrenal gland (3%). Of all patients with stage IV melanoma, 39 (20.7%) had prolonged survival of 2 years or longer and 17 patients of long-term survivors (43.5%) underwent metastasectomy. The 2-year, 5-year and 10-year survival rates were 16.5%, 2.6%, and 1.6%, respectively. As evaluated by logistic regression, of all the modalities of therapy given, only surgery correlated with prolonged survival ($p < 0.0001$). The current study failed to show that systemic chemotherapy alone significantly influenced survival, but the combination of surgical and chemotherapic treatment resulted in the longest median survival time (192 months).
Conclusions: Survival of patients with advanced melanoma is generally poor, but there are occasional long-term survivors. The current analysis demonstrates that of the modalities of therapy given, only surgery significantly influences survival. We conclude that a surgical resection of limited number of metastasis, especially with a long relapse-free interval, may influence the course of stage IV melanoma and contribute to prolongation of life: therefore, when technically feasible, it should be the first option. However, in selected cases, a multimodal approach can result in a long-term disease control.

7020 POSTER

Uveal melanoma – a single center multidisciplinary experience between 2000 and 2006

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Background: The clinical course and outcome of uveal melanoma are not well described and the ocular presentation of melanoma and its prognostic factors differ in many ways from the cutaneous form. We evaluated the survival of patients (pts) with uveal melanoma, factors that correlate with survival and evaluated the clinical response to local and systemic therapy.
Materials and Methods: All pts with uveal melanoma followed at IPOLFG between 2000 and 2006 were identified from our database. We recorded date of diagnosis, therapeutic approaches, date of metastatic disease, site of the first metastasis, date of last follow-up and outcome.
Results: We identified 72 pts (71% male) with uveal melanoma, with a median age of 54 years. All pts were caucasian. Twelve percent of pts had metastatic disease at diagnosis; the median survival in this group was 11 months and prognosis was poorer in older pts. Seventy nine percent of pts with local disease were treated with proton beam radiotherapy in a specialized center outside our Institution. Enucleation was reserved for pts with a bulky disease and a contralateral healthy eye or invasion of the optic nerve. Thirty eight percent of pts developed metastatic disease and almost all had a single organ as the site of first metastasis. Liver involvement was documented in all pts with advanced disease. Systemic disease was managed with Dacarbazine and Fotemustine upon progression.
Conclusions: Uveal melanoma represents a continuous challenge for oncologists. Many pts with uveal melanoma were referred from outside our Institution. This analisys shows a slightly inferior incidence of metastatic disease than usually referred in literature. A timely multidisciplinary approach may be considerered an important factor in the disease outcome. The impact of local therapy on quality of life, as well the lack of effective drugs for systemic disease, makes this disease an appealing target for new approaches.

7021 POSTER

Paired intra-patient pharmacokinetic study of oblimersen in combination with dacarbazine in metastatic melanoma

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Background: An oblimersen (Obl) plus dacarbazine (DTIC) regimen was studied in a large phase III trial in metastatic melanoma and was shown to be superior to DTIC alone on several efficacy endpoints (RR 7.5% vs. 13.5% [$p < .01$], median PFS 1.6 vs. 2.6 months [$p < 0.001$], median OS [$p = 0.077$]). Obl has a short plasma half-life of about 2 hours; however, in animal studies, intracellular tissue concentrations have been shown to persist for several days. Obl is metabolized by nucleases present in most tissues, including the liver. DTIC is a prodrug that is metabolized in the liver by cytochrome P450 isoform 1A2 (CYP1A2) to form the N demethylated metabolite. This metabolite rapidly decomposes to form amino-imidazole carboxamide (AIC) and the reactive methylating species. As Obl weakly inhibits CYP1A2 (Ki= 6 microM), a study was designed to evaluate the potential drug-drug interaction.
Methods: Patients with metastatic melanoma were randomly assigned to receive either DTIC as a single agent in the first cycle and the combination of DTIC and Obl in the second cycle, or the reverse sequence. The interval between cycles was 3 weeks. Further treatment was allowed at the discretion of the investigator based on response. Obl 7 mg/kg/day was administered as a continuous infusion for 5 days with a pump on an outpatient basis followed by a 1-hour infusion of DTIC 1000 mg/m^2. Plasma Obl concentration was evaluated at time 0, 24 h and 96 h after the start of the infusion, at the end of infusion (EOI), and 1 h, 2 h, 3 h, 5 h, and 7 h after EOI. DTIC and AIC concentrations were evaluated at time 0, 55 min after the start of the infusion, and 5 min, 15 min, 30 min, 1.5 h, 3 h, and 6 h after EOI. Key exclusion criteria were ongoing corticosteroid treatment and active smoking.
Results: Sixteen patients have been enrolled to date, and results will be presented.
Conclusion: This study design allows inter- and intra-patient comparison of PK parameters for Obl and DTIC and assessment of correlative clinical endpoints.

7022 POSTER

High dose interferon alpha 2b as adjuvant therapy in high-risk resected malignant melanoma: 10 year experience of patients treated in Northern Ireland

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Background: High-dose interferon alpha 2b (HDI) improves relapse free survival (RFS) in patients with high-risk resected malignant melanoma in large prospective North American trials. There has been little published experience of HDI use in the UK or Europe. We have retrospectively reviewed the use of HDI in Northern Ireland over a 10 year period.
Materials and Methods: We reviewed all patients with malignant melanoma who received adjuvant HDI from 1st January 1996 to 31st December 2005 in the Northern Ireland Cancer Centre (NICC) with respect to patient characteristics, tumour stage, toxicity, and outcome. Patients were planned to receive 20 MU/m^2/d intravenously (IV) for 4 weeks and 10MU/m^2 three times per week subcutaneously (SC) for 48 weeks as per the landmark ECOG 1684 trial.
Results: During the 10 years 639 patients with malignant melanoma were referred to the NICC. 72 patients received adjuvant HDI. Median patient age was 46.5 years. 53% of patients were female and 89% of patients were performance status (PS) 0, 11% PS 1.
The most common tumour site was the lower limb (40.3%), followed by the trunk (23.6%). 18% of patients were node negative (all IIB/IIC) and 82% node positive at the time of treatment. HDI was given following surgery for initial presentation in 43% of patients and following surgery for disease relapse in 57%. Disease relapse was mainly nodal although 3 patients received HDI after resection of metastatic disease.
All patients ($n = 72$) had the IV treatment phase. 39% of patients required a dose delay or dose reduction. 89% of patients completed all planned treatments.
15 patients did not proceed to SC treatment (3 relapsed, 3 toxicity, 9 clinical trial protocol). 53% starting SC treatment completed all planned treatment. Overall 65% of patients experienced Grade 3 or higher toxicity. 1 patient with thrombocytopenia died of an intracranial haemorrhage whilst on SC treatment (platelets 113x109/l).
The median follow-up is 2.00 years (range 0.44−8.7 yrs). 31 (43%) patients have relapsed and 20 (28%) have died. The median RFS is 3.15 years. The median overall survival (OS) has not been reached. The 1, 2 and 5 year OS rates are 87%, 74% and 61% respectively.
Conclusions: High dose interferon can be delivered in a regional UK cancer centre with toxicity and outcomes comparable to that seen in large prospective randomised controlled trials.