Methods: Prospective database study of 262 consecutive sentinel node procedures in primary melanoma patients, (primary: Breslow thickness >1 mm and/or ulceration, and/or Clarke level IV) treated between 1997 and 2004. Histopahologic work up of the SN according to the EORTC Melanoma Group protocol (Cook MG et al, J Pathol. 2003 Jul; 200(3): 314–9). Analysis of DFS and OS was performed using the Kaplan-Meier approach. Multivariate and univariate analysis using the Cox's proportional hazard regression model were performed to assess the prognostic value of covariates with respect to DFS and OS.
Results: At least one SN was harvested in each patient. Median follow-up was 23.3 months. In 77 patients the SN contained metastatic melanoma cells (29%). The established false-negative rate during follow-up was 9.4%. Patient factors that determined SN status were Breslow thickness and ulceration. Patient factors that influenced disease-free survival were SN status, location and ulceration of the primary tumor. Overall survival was influenced by SN status and ulceration of the primary tumor. Locoregional recurrence was 6.5% in SN negative patients versus 22.1% in SN positive patients ($P < 0.001$). The distant recurrence rate was 3.8% in SN negative patients versus 27.3% in SN positive patients ($P < 0.001$). The in-transit metastasis rate correlated with SN-positivity, Breslow thickness and ulceration. Actuarial 5-year overall survival rate in SN negative patients was 93% and in SN positive patients 51% ($P < 0.001$).
Conclusions: The SN procedure is a reliable and accurate procedure and SN status is the most important predictive factor for DFS and OS. Our findings confirm that the EORTC Melanoma Group SN work up protocol detects SN positivity in about 30%, which is substantially higher than most procedures reported in the literature (average of 18%). Breslow thickness and ulceration are both factors influencing SN status. SN positive patients have a significantly increased risk to develop any form of locoregional or distant recurrence compared to SN negative patients.

1193 ORAL

Quantitative RT-PCR (qRT) based analysis of tyrosinase, MART-1 and MAGE-A3 in Sentinel Lymph Nodes (SLNs) from Malignant Melanoma (MM) patients

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Background: Detection of micrometastases in SLNs is critical for staging of melanoma. When SLNs are involved, survival is reduced in 40%, nevertheless, prediction of outcome is imprecise with conventional techniques. We and others have found that detection of a higher number of tumor-specific molecular markers in melanoma SLNs may identify patients with an increased risk of recurrence. We have compared the results of this analysis using different criteria: the classical numerical criterium and the presence of specific combinations of markers.
Material and methods: 157 pts with cutaneous melanoma 0.75 mm Breslow thickness underwent SLN biopsy. A portion of each SLN was stored frozen at −80ºC and assessed by qRT for mRNA of three genes: MART-1 (antigen recognized by T cells-1), MAGE-A3 (melanoma antigen gene-A3 family) and tyrosinase.
Results: Twenty-five (15.9%) pts had histologically positive (HISTOL+) SLN. Marker expression for Tyrosinase, MART-1 and MAGE-A3 in HISTOL+ and HISTOL− pts were as follows: 92%, 72%, 36% and 77%, 35%, 11%. All individual markers and their combinations had prognostic significance for DFS in the crude analysis. Nevertheless, in the multivariate analysis no single marker had prognostic significance, only the criteria of "two or more positive markers" ($HR = 2.37$, $p = 0.036$), as well as the "simultaneous positivity of tyrosinase and MART-1" ($HR = 2.35$, $p = 0.038$) were independent prognostic factors. Pearson correlation test found a significant correlation between these two criteria ($r = 0.919$; $p < 0.001$). Numerical criteria using "two or more positive markers" and the criteria of "simultaneous positive tyrosinase and MART-1" identified 66 pts (42%) and 60 pts (38%), respectively. Risk scores for each individual could be calculated by a risk equation derived from the regression model with a sensibility of 63% and a specificity of 68% (area under the ROC curve of 0.836).
Conclusions: Multimarker qRT is an useful molecular staging test that may more precisely identify patients with higher risk of recurrence. Patients with positive SLNs for two or more markers have a higher risk of recurrence, and these patients were mainly those who were positive simultaneously for tyrosinase and MART-1. It suggests that a more simple assay avoiding MAGE-A3 could be use with similar results.

Poster presentations (Mon, 31 Oct)
Melanoma and sarcoma

1194 POSTER

Uveal melanomas treated BZ gamma knife

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Purpose: To analyse treatment results, complications and prognostic factors for survival of patients irradiated for uveal melanomas using the Leksell gamma knife
Material and methods: During 8 years 126 patients with uveal melanomas were irradiated using the Leksell gamma knife. The median of gross tumor volume (GTV) was 551 mm^3(33–7800 mm^3), the median of planning treated volume (PTV) was 1,300 mm^3(67–8200 mm^3), the median of tumor height was 8 mm (1–20 mm). The median of minimal single dose (Dmin) was 34 Gy (28–85 Gy). Patients were followed by an ophthalmologist at regular intervals, magnetic resonance was performed every 12 months. Tumor regression was defined as a decrease in tumor height registered by A and B ultrasonography scans and by control magnetic resonance imaging. The minimal follow up for survivors was 24 months. The SOMA LENT scoring system was used to measure radiation induced side effects.
Results: *1. Local tumor response*. The complete or partial tumor regression can be achieved in 70% of patients. The maximum local effect has been recorded after the interval of 20–30 months since the treatment (see the figure).
2. Toxicity. The most common late toxicity were: retinopathy, cataracts, secondary glaucoma and optic neuropathy. The median time to occurrence of secondary neovascular glaucoma was 18 months and we did not observe any significant influence of the minimum dose and tumor location, but a significantly lower incidence of secondary glaucoma was noticed when the volume of PTV was less than 1,000 mm^3 with an incidence 6.9%. In the analysis of late toxicity we recorded the following results: significantly lower toxicity in the optic nerve was observed when the maximum dose was less than 10 Gy (incidence of grade 3, 4 only in 2.4%), in the cornea when maximum dose did not exceed 10 Gy (incidence of toxicity 3, 4 in 3%), in the lens when the maximum dose did not exceed 7 Gy (incidence of toxicity grade 3, 4 in 7.7%) and in the iris when the maximum dose did not exceed 15 Gy (incidence of 3, 4 grade late toxicity in 4.6%).
3. Prognostic factors and survival. Patients younger than 50 years have the best prognosis, with a pre equatorial location of the tumor, when tumor height did not exceed 5 mm, GTV was not larger than 500 mm^3 and there was no other organ dissemination.
Conclusion: The acceptable incidence of late toxicity for all eye critical structures was observed when the maximum dose to these structures did not exceed 10 Gy and effective local tumor response was achieved in 70% of patients. The stereotactic irradiation can extent conservative therapeutic options for these types of tumors with visus or eye preservation.

1195 POSTER

The role of adjuvant radiation therapy in uterine sarcoma

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Background: The aims of this retrospective single institution case series analysis are to investigate prognostic factors regarding overall survival (OS), cause-specific survival (CSS), relapse-free survival (RFS), and loco-regional relapse-free survival (LR-RFS), and to evaluate the role of adjuvant radiotherapy (RT) in uterine sarcomas.
Patients and methods: From 1984 to 2004, 198 patients with uterine sarcoma were treated at the Istituto Nazionale Tumori. The distribution by histology was the following: leyomiosarcoma (LMS)=95; smooth muscle tumors of unknown malignant potential (STUMP)=9; endometrial stromal sarcoma (ESS)=40; malignant mixed mullerian tumors (MMMT)=34; adenosarcoma (AS)=10; other mesenchymal types=10. Stage distribution according to FIGO (as modified by Salazar-Cancer 1978; 42:1152–60) was as follows: stage I=127; stage II=18; stage III=22; stage IVa=16; stage IVb=15. All the 167 stage I-III patients underwent surgery; 33 patients were given adjuvant chemotherapy and 45 patients were given adjuvant pelvic RT. The mean delivered dose was 54 Gy with conventional fractionation. OS, CSS, RFS and LR-RFS were calculated according to the Kaplan-Meier method. The level of significance was evaluated with the Log Rank test; the proportional hazards model of Cox was used for the multivariate analysis. Acute and late toxicity were scored according to the RTOG grading system.
Results: 5-year OS and CSS were 56% and 48.7%, respectively. RT was not a significant prognostic factor for OS, CSS or RFS, while it turned out