the overall survival with mostly unsatisfactory results. In this study we evaluated the efficacy of a combined chemo-/hormonal therapy with dacarbazine (DTIC) and tamoxifen (TAM).

Methods and Results: 23 melanoma patients (14 women and 9 men; median age 58 years, ranging from 35 to 81) with multilocular metastatic disease were treated with DTIC/TAM. Organs most often affected were skin, lung, lymph nodes and liver. In 5 patients (21.7%) DTIC/TAM was applicated as first line therapy. The patients received 250 mg/m^2 DTIC i.v. and 20 mg/m^2 TAM p.o. for 5 consecutive days every three weeks; staging was performed after 2–3 cycles. An average of 4 cycles (1–16) was administered. 8 patients (34.8%) showed stable disease after 3 and for 1–13 more cycles of DTIC/TAM whereas complete or partial remissions could not be reached. The overall survival rate for those patients, who obtained DTIC/TAM as first line therapy, was 3 months (2–13 months) and 6 months (1–38 months) for the pretreated collective respectively. Serious toxicities were not observed.

Conclusion: In our hands the overall response and survival rates of 23 melanoma patients treated with DTIC/TAM were lower than previously reported. This may be due to a worse performance status with high tumor burden even in patients, who received DTIC/TAM in first line. Furthermore we could not observe a significant survival benefit for women compared to men treated with this regimen.

1171 POSTER

Prognostic meaning of DNA ploidy in malignant melanoma and pigmented nevi

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Purpose: The determination of DNA content in human cancers is the subject of increasing interest, particularly in view of its potential clinical applications. There are relatively few conflicting studies which describe DNA content of melanoma and pigmented nevi.

Methods: DNA ploidy was measured using flow and video-imaging cytometry in 103 malignant melanomas and 61 pigmented nevi. For DNA measurement paraffin embedded tissue and fresh cells smears were used. Clinical and histological data of malignant melanoma were recorded and correlated with DNA ploidy.

Results: Aneuploidy rate was significantly higher in whole malignant melanoma group, in clinical stage II and III, in tumors with thickness greater then 1.5 mm, tumors with Clark level III, IV and V. In the whole population of pigmented nevi aneuploid DNA content was identified in 14 nevi (23.0%).

Conclusions: Results suggest that aneuploidy seems to be connected with advanced stage of malignant melanoma but it does not replace other prognostic factors. Both cytometric methods can be used for routine DNA ploidy analysis. Results obtained from fresh cells smears and paraffin embedded tissue were identical.

1172 POSTER

Does polychemotherapy with dacarbazine, vindesine and cisplatin represent a useful therapeutic alternative in patients with advanced melanoma?

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Purpose: In patients with metastatic melanoma different therapeutic concepts have been administered but response rates observed are still low. In a retrospective study the response to combination chemotherapy comprising of Dacarbazine, Cisplatin and Vindesine (DVP; EORTC schedule), was analysed.

Method: 51 patients with advanced melanoma (21 women and 30 men; median age 53 years; 43 pretreated) treated with DVP at the Dpt. of Dermatology, University of Heidelberg from 1992–1996 were analysed retrospectively.

Results: We observed an overall response rate of 9.8% consisting of 0 CR and 5 PR. In our patients the PR lasted 7 (5–10) months. The overall efficacy of this protocol including all patients achieving either CR, PR, MR and SD was 35.3%. The overall survival for all patients from the beginning of treatment was 8.2 (1–29) months. However, there was a marked difference in the overall survival rates for the patients responding to therapy 15.0 months versus 5.6 months in patients with PD. Toxicity observed was rather mild included polyneuropathy 6/51 thrombocytopenia 4/51 alterations in renal function 2/51 and persisting emesis 1/51 treatment had to be discontinued in only 3 patients.

Conclusion: Considering the efficacy of 35.3% achieved in our patients and the moderate toxicity observed this protocol remains a treatment alternative in patients with metastastic melanoma.

1173 POSTER

Nucleolar organizer regions (NORs), mitotin expression, and caseine kinase II (CKII) activity in melanocytic naevi and malignant melanomas

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Purpose: To evaluate the degree of "proliferative activity" in cutaneous melanocytic tumors using three different methods.

Methods: Argirophil technique for staining the NORs and two-step immunoperoxidase method with monoclonal antibody against 125 kD/pI 6.5 PCNA/mitotin were applied on a variety of 40 melanocytic formalin-fixed, paraffin-embedded specimens. CKII activity, after Mono Q column, was monitored with [γ-32P]GTP and its specific substrate RRREEETEEE; spermine, polylysine, heparin, poly (Glu-Tyr) 4:1, quercetin, and 2,3-bisphosphoglycerate were used for identification.

Results: A significant difference between the number of NORs per cell in benign and malignant lesion as a group was shown, but some overlapping counts were found. Mitotin was expressed in significantly higher degree in metastatic and primary melanomas compared to common and dysplastic naevi. CKII activities from melanomas and dermal naevi were 5.9 and 2.5 fold higher than from the normal skin.

Conclusion: Metastatic and primary melanomas showed a higher degree of proliferative activity compared to dysplastic and common naevi. The monoclonal antibody against mitotin is suit for determinating the proliferating fractions on paraffin sections. CKII probably takes central role in transformed and non transformed skin proliferations.

1174 POSTER

Increased serum levels of soluble receptor for tumour necrosis factor p-55 in melanoma patients

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Purpose: Soluble forms of the cell surface receptors for tumour necrosis factor have been detected in the serum and urine. Concentration of soluble tumour necrosis factor receptor (s-TNF-r) p-55 is elevated in the serum of pts with infections, trauma and cancer. The aim of this study was to quantify serum level of p-55 and to prove their prognostic value in metastatic melanoma.

Methods: Serum level of sTNF-r p-55 were measured in 69 healthy donors (group A), 31 melanoma pts without evidence of disease at least 30 MOs after surgical excision of primary melanoma (group B) and in 47 metastatic melanoma pts before chemoimmunotherapy and before each cycle of treatment (group C). P-55 was determined with enzyme-linked immunosorbant assay (ELISA), developed at Blood Transfusion Centre of Sovenia.

Results: Mean concentration of p-55 in group A, B, C was 0.5, 0.4, 2.1 ng/mL respectively ($p = 0.06$). In group C, the concentration of p-55 in 18 responders and 29 non responders were 0.16 and 3.3 ng/mL ($p = 0.001$); during treatment, no significant changes of concentration were noticed.

Conclusion: The serum concentration of p-55 is elevated in metastatic melanoma pts and may predict the treatment results.

1175 PUBLICATION

Uveal melanoma (UM) I. 125 brachytherapy: Indications, technique and preliminary results

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Purpose: We presented our experience from sept. 96, with I. 125 plaques in conservative treatment of UM, indications, dosimetry, and surgical implantation.

Methods: We have treated 10 pts. with UM, less than 10 mm height, without evidence of metastases. Preliminary dosimetry was performed with BEBIG program. COMS plaques diameters was 14–22 mm (2 mm margin tumor). The dose was always referred to tumor apex. Average: dose was 88 Gy, dose rate 80 cGy/h. Surgical implant was made in the brachytherapy theater under general anesthesia. After to open yuxtacorneal conjuntiva, transilumination exploration and previous sutures was performed and definitive implant placed. In 9 cases was necessary to remove the rectus m. Minimal follow up: 6 months.

Results: Tolerance was good. Acute conjuntivitis was normal and controled with topical treatments.

Conclusion: Epiescleral I. 125 plaques is elective conservative treatment for UM. Brachytherapy is feasible. More follow up and number of pts. is necesary to know local control rate and late effects.

1176 PUBLICATION

RT-PCR detection of melanoma cells in peripheral blood stem cell harvests of patients with metastatic malignant melanoma

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The objective of this study was to develop a sensitive multimarker polymerase chain reaction assay to detect melanoma cells contaminating peripheral blood stem cell harvests (after G-CSF 2 × 5 μg/kg daily times; 4–5 days) of patients with progressive metastatic malignant melanoma. The melanocyte-specific transcripts of tyrosinase and Melan-A/MART-1 as well as the tumor-specific transcript of Mage-3 were used as molecular markers to detect neoplastic cells in eleven metastatic malignant melanoma patients to be treated with high-dose chemotherapy and autologons peripheral stem cell support (Table).

Table: Patient characteristics and results

Patient	Sex/Age (yr)	RT-PCR results: Tyr/MART-1/Mage-3	Metastatic Sites
A	f/27	−/−/−	ST, bone
B	m/26	−/−/−	cutaneous, lymph, pulm
C	m/55	−/−/−	ST, lymph
D	m/47	−/−/−	pulmonary (bulk)
E	m/45	−/−/−	pulm, lymph, liver
F	f/48	−/−/−	lymph, liver, SC
G	m/25	−/−/−	SC, pleural, lymph
H	f/39	−/−/−	lymph
I	m/38	+/−/+	lymph, liver, spleen
J	f/43	−/−/−	lymph, SC
K	m/35	−/−/−	lymph, liver

ST = soft tissue, SC = subcutaneous, lymph = lymphatic, pulm = pulmonary, Tyr = tyrosinase.

With a sensitivity of the nested tyrosinase reverse transcriptase-polymerase chain reaction (RT-PCR) method to detect one melanoma cell in 2 × 10^6 peripheral blood mononuclear cells, only one patient's stem cell harvest tested positive for tyrosinase and Mage-3 message. All harvests were negative for Melan-A/MART-1, which result may be due to a ten-fold and five-fold lower sensitivity of detection when compared to tyrosinase RT-PCR and Mage-3 RT-PCR, respectively. Our results suggest that melanoma cells usually are not mobilized into peripheral blood to a significant degree following G-CSF application

1177 PUBLICATION

Metastatic ocular melanoma – Experiences with chemoimmuno-/polychemotherapy

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Purpose: At the Dept. of Dermatology, University of Heidelberg, between 1991 and 1996 32 patients (pts.) (14 females, 18 males, median age 55 years) with ocular melanoma were seen. 30 pts. had uveal and 2 conjunctival melanoma. 8 of 32 pts. (25%) are free of disease for 34 months (mo.) median, 24 pts. progressed and most developed multilocular metastases e.g. in liver (87.5%), subcutaneous tissue (33.3%) and lymph nodes (20.8%). In 7 pts. liver metastasis represented the only site of metastatic disease.

Methods and Results: 21 pts. with metastatic disease either received chemoimmunotherapy with Dacarbazine (DTIC) and Interferon α (IFN) or polychemotherapy consisting of DTIC, Cisplatin and Vindesine (DVP). DTIC/IFN was given to 13 pts.. No complete or partial responses (CR, PR) could be obtained. Stable disease (SD) lasting 3.5 mo. was achieved in 4 pts. Median survival of first line treated pts. was 9 mo. and of pretreated pts. 6 mo.. DVP was given to 13 pts., neither CR, PR or SD could be achieved. Median survival of first line treated pts. was 6 mo. and of pretreated pts. 4 mo..

Conclusion: These results once more demonstrate that therapeutic concepts that can achieve response rates of up to 53% in metastatic *cutaneous* melanoma are of little benefit in metastatic *ocular* melanoma.

1178 PUBLICATION

Oral etoposide in patients (pts) with Kaposi's sarcoma (KS)

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Purpose: Etoposide (E) has been used in the treatment of a wide variety of neoplasms, including KS. The best therapeutic approach is still unclear. We herein report the preliminary results of a phase II trial of oral E in generalized and progressive Kaposi's Mediterranean sarcoma (4 pts) and KS developed under immunosupressive therapy (4 pts).

Methods: Between September 1993 to March 1996, 8 patients (pts) with biopsy confirmed progressive KS were accrued. All pts were HIV (−). Median age was 43 yrs (range 31–67). Five pts had received prior treatment; with RT (3), RT and chemotherapy (1) or chemotherapy (1). 3 pts had renal transplantation and 1 pt had pemphigus vulgaris. All pts had stage II disease. Oral E was given at the dose of 50 mg bid for 10 days every 21 days. All pts completed at least 2 cycles, 6 pts received more than 4 cycles (range 2–9). During E treatment pts with renal transplantation had been using azathioprine and prednisone.

Results: In three pts with renal transplantation, grade III neutropenia were developed. No other grade III and IV toxicities were detected. Of the 8 pts, 1 pt required dose reduction of 25% and 2 pts delay of at least 1 week due to hematological toxicity (in pts with renal transplantation). 7 pts achieved a complete response (87%) which continue for 3, 8+, 8+, 11+, 14+, 18+, 29+ months, respectively. After completing chemotherapy all these 7 pts are still alive. In 1 pt with previous chemotherapy and renal transplantation minimal regression was detected. This pt died 4 months after completion of chemotherapy because of a cardiac reason.

Conclusion: In pts under immunosupressive therapy, main toxicity is hematologic. It may be concluded that oral E is effective for use in pts with generalized and progressive Kaposi's Mediterranean sarcoma or KS developed under immunosupressive therapy.

Lymphomas

1179 ORAL

Clinical activity of the monoclonal antibody (MAB) IDEC-C2B8 in patients (pts) with relapsed low-grade or follicular NHL (R-LG/F NHL)

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Purpose: We conducted a single-agent, multicenter, clinical trial (PIII) in a total of 166 pts with R-LG/F NHL (IWF classes A, B, C, D), treated with IDEC-C2B8 at 375 mg/m^2 weekly for 4 infusions to establish safety and efficacy of the MAB.

Pt characteristics: Gender – 61 F/105 M, median age – 57 years, median time since diagnosis – 4.1 years, stage at diagnosis – 78% III/IV, prior chemotherapy – median 2 relapses.

Results: Adverse events (AEs) were primarily related to 1st infusion and usually consisted of fever, chills, nausea, and headache. Only 34 pts had grade 3, and five pts had grade 4 treatment-related AEs (usually transient and reversible). There were no treatment-related deaths. Incidence of HACA was <1% and not associated with AEs. In the 166 pts, the overall response rate (ORR) was 48% (6% CR and 42% PR). Evaluable pts (151/166) had an ORR of 50% (6% CR and 44% PR). Responses (CT scans) were confirmed (blinded audit) by an independent panel of lymphoma experts (LEXCOR panel) using established response criteria. Median time to progression for responders has not been reached (9+ mo median follow-up). The ORR in