

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 multilocal 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 applied as first line therapy. The patients received 250 mg/m<sup>2</sup> DTIC i.v. and 20 mg/m<sup>2</sup> 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.

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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 than 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.

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### 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 metastatic melanoma.

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### Nucleolar organizer regions (NORs), mitotin expression, and casein 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:** Argiophil 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 [ $\gamma$ -<sup>32</sup>P]GTP and its specific substrate RRREEETEE; 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 determining the proliferating fractions on paraffin sections. CKII probably takes central role in transformed and non transformed skin proliferations.

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### 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 chemioimmunotherapy and before each cycle of treatment (group C). P-55 was determined with enzyme-linked immunosorbent assay (ELISA), developed at Blood Transfusion Centre of Slovenia.

**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.

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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.