The drug SnET2 was intravenously injected and subsequently activated, 24 hours post-injection, by 665 nm light delivered via fiberoptic from a diode laser light source. The total light dose delivered was 300 J/sq.cm at a power density of 150 mW/sq.cm. Response rates were assessed by serial follow-up and patient subjective satisfaction rates were recorded.

Results: Subjectively each patient was satisfied with the cosmetic outcome of treatment. Of 8 evaluable patients with 116 lesions objective response rates were: (CR 75%; PR 19%; NR 0%; 6% of lesions were of indeterminate status at follow-up). Follow-up ranged from 1–9 months. Adverse experiences were mild to moderate of which 100% were due to sun exposure and did not require treatment.

Conclusions: PDT is a well tolerated procedure that produces excellent subjective and objective responses. The patient is treated in a single session on an outpatient basis. PR and new or recurrent lesions can be retreated with PDT without complications or the development of resistance to therapy.

1162 POSTER

Optimized detection of 5-S-cysteinyldopa (5-S-CD) in serum of melanoma patients: A new marker of metastatic melanoma

E. Stockfleth, J. Hartleb, T. Meyer, O. Heckmann, R. Arndt, E. Christophers, A. Hauschild. *Department of Dermatology, University of Kiel; IPM-Hamburg, Germany*

Purpose: It has been tried for years to establish a specific prognostic serum marker of malignant melanoma, which correlates with the clinical aspect of the patients. The routine use of 5-S-CD as a marker of melanoma progression, has been discussed controversially in the literature.

Methods: We investigated 58 melanoma patients (22 females, 36 males) with a total number of 77 serum samples. The patients were in different clinical stages (I–IV): primary tumors (I/II; n = 20); locoregional metastasis (III; n = 14); as well as advanced metastatic disease (IV; n = 21). 5-S-CD was collected under special antioxidative conditions, measured by a new optimized HPLC-analysis which makes the test useful for routine diagnosis.

Results: In healthy controls as well as in patients with other tumor entities, 5-S-CD remained within the normal range (< 1.6 μg/l). 5-S-CD serum level >1.6 μg/l could be detected in 35.6% of our patients in stage III and 87% in stage IV. We found clearly positive values for 5-S-CD (>3.2 μg/l) in stage I+II = 5%; stage III = 21.4%; stage IV = 57.1%. Increased levels of 5-S-CD correlate with the tumor mass and location of the metastases (visceral vs. non-visceral).

Conclusion: This new optimized HPLC-method to detect serum levels of 5-S-CD enables us to establish a promising tumor marker for the clinical state of melanoma patients. Our testsystem provided to be of high specificity and sensitivity and could be useful in the routine diagnosis and therapy monitoring.

1163 POSTER

Essential factors in hyperthermic isolated limb perfusion (HILP) – Experimental results of in-vitro and in-vivo studies

Th. Meyer, J. Göhl, W. Hohenberger, I. Muckenschnabel[1]. *Department of Surgery, University Hospital Erlangen-Nuremberg; [1]Institute of Pharmacy, University of Regensburg, FRG*

HILP for regionally metastasizing malignant melanoma of the extremities is a complex method of treatment influenced by multiple factors like temperature, drugs, drug administration modes, duration of perfusion etc. Several of these parameters were investigated in different experimental models.

Temperature-dependent intracellular uptake of melphalan (L-PAM) in a human melanoma cell line (SK-MEL-24) was measured by high-performance liquid chromatography (HPLC). A temperature rise from 37 to 41.5°C increased cellular melphalan uptake 16-fold. Further enhancement of temperature from 42 to 43°C decreased the cell-associated melphalan to the level at 37° indicating a carrier-mediated melphalan uptake also in melanoma cells. Additive effects of melphalan and hyperthermia seemed evident.

Using a miniature equipment for the perfusion of rat limbs we examined the impact of temperature, duration of perfusion and drug administration on tissue uptake of L-PAM. The highest tissue concentrations, measured by HPLC, were observed when perfusion was performed over 90 minutes with temperatures between 40.5°C and 41.5°C and the drug administered continuously into the arterial line within 20 minutes.

Since experimental in vitro- and nude mice studies showed an excellent effect of vinblastine on human melanoma it was considered for experimental extremity perfusion. Normothermic (37°C–38°C) vinblastine perfusions were performed on melanoma bearing nude rats (SK-MEL-3). HPLC-analysis of vinblastine concentrations in tissues (skin, muscle, tumor) demonstrated an increasing uptake of the drug during the course of perfusion. After microsurgical restoration of the vessels complete tumor regression was observed in single surviving animals.

These results suggest that experimental studies can help to clarify essential factors in HPLC. Potential consequences for clinical HILP are addressed.

1164 POSTER

Soluble VCAM-1 as predictor of survival in patients with advanced malignant melanoma

J. Atzpodien, A. Franzke, M. Probst-Kepper, J. Buer, M. Volkenandt, F. Wittke, R. Hoffmann, A. Ganser. *Department of Hematology and Oncology, Medizinische Hochschule Hannover, 30623 Hannover, Germany*

Very rapid progression of disease with a median of 6 to 9 months is a common feature of metastatic malignant melanoma. Nevertheless, substantial variability of survival suggests that metastatic malignant melanoma can be divided into several biologic subgroups. We evaluated serum levels of soluble adhesion molecules (soluble vascular cell adhesion molecule-1 = sVCAM-1; soluble intercellular cell adhesion molecule-1 = sICAM-1; soluble endothelial leukocyte adhesion molecule-1 = sE-Selectin) and various clinical parameters (e.g., sex, visceral metastases, liver metastases, lactate dehydrogenase, erythrocyte sedimantation rate, C-reactive protein) in 97 consecutive patients with metastatic malignant melanoma seen at our institution between May 1990 and April 1996 and assesed their prognostic value. For statistical analysis, we used both univariate and multivariate Cox proportional-hazards models. Elevated serum levels of sVCAM-1 ($p = 0.02$) and of lactate dehydrogenase ($p = 0.0002$) were rendered statistically independent and were significantly associated with unfavourable outcome. Patients were assigned to one of three risk categories according to a cumulative risk score defined as the function of the sum of these two variables. There were significant differences in overall survival ($p < 0.0001$) between low (n = 53; median survival of 17 months), intermediate (n = 29; median survival of 6 months) and high risk (n = 15; median survival of 4 months) patients. Elevated serum levels of sVCAM-1 and of lactate dehydrogenase correlate with poor outcome in metastatic malignant melanoma. These data support risk stratification for future therapeutic trials, and identify factors which may influence decision making in palliative management of patients with disseminated malignant melanoma.

1165 POSTER

Treatment of metastatic melanoma with a combination of carmustine, dacarbazine, cisplatin, tamoxifen and interferon alpha

N. Haim[1], Z. Bernstein[1], Z. Shklar[1], M. Steiner[2], M.E. Stein[1]. *[1]Department of Oncology, Rambam Medical Center; [2]Department of Oncology, Lin Medical Center, Haifa, Israel*

Purpose: The combination of carmustine, cisplatin, dacarbazine and low-dose tamoxifen (20 mg/day) is widely used in metastatic melanoma (MM), and was originally reported to induce 55% objective response (OR) rate and 20% complete response (CR) rate (Cancer Treat Rep 68:1403, 1984). We evaluted a similiar combination but one to which interferon alpha (INF) was added.

Methods: INF 6×10^6 units/m^2/day was given subcutaneously on days 4–8 and 17–21 every 3 weeks. The other drugs were given as originally described. Eligibility criteria included WHO PS 0–3 and measurable disease.

Results: 30 patients (pts) were entered in the study. Among 29 evaluable pts, OR was seen in 15 (52%) and CR in 5 (17%). Median duration of partial response was 4 mo (range, 1–12+ mo) and of CR was 8 mo (range, 2–14+ mo). CR continues in 2 pts with lung metastases at 10+ and 14+ mo. Median survival time was 8.7 mo. Median WBC nadir was 2,050/mm^3 and median platelets nadir was 29,000 mm^3. Neutropenic fever developed in 4 (13%) and platelets transfusions were required in 5 (17%). One patient died with neutropenia and sepsis. Due to thrombocytopenia, the median interval between the first 2 courses was 4 weeks (instead of 3 weeks) and drug doses were reduced in the second course in 8/26 (31%).

Conclusion: The above-noted drug comination is active in MM and may induce durable remission. However, due to severe thrombocytopenia, a reduction of carmustine dose is recommended.