ABSTRACTS

FC24
Therapeutical Experience in Classic Kaposi's Sarcoma
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In 28 years' experience we observed 550 classic Kaposi's sarcoma patients. Many of them underwent local and/or systemic chemotherapy. On the basis of such a large survey we had the opportunity to develop a clinical staging system in order to decide the therapeutical strategy, useful especially in older and impaired patients. In initial stages (I and II with slow progression) we prefer clinical observation, intralesional chemotherapy (vinristine) for isolated nodules, radiotherapy in selected cases and compression with elastic stockings. In stages II with fast progression, III and IV, basic therapy is systemic mono- or polychemotherapy, with compression with elastic stockings as a useful support. As first-line therapy we use: Vinblastine: induction 4, 6, 8 mg i.v. weekly, maintenance 10 mg i.v. every 3 weeks Vinblatine + Bleomicine 15 mg i.m. every 2 weeks after vinblatine induction. As second-line therapy: Vinorelaine: induction: 17.5 mg/m² every 2 weeks for 5 cycles; maintenance 29 mg/m² every 3 weeks. Etoposide 150 mg/die i.v. for 3 consecutive days every 3 weeks. Gemcitabine 1200 mg/m² i.v. weekly for 2 weeks followed by a three-weeks interval. Epirubicin 20 mg i.v. weekly. All these chemotherapies have to be maintained up to the best clinical result as negative.

FC25
Sentinel Node Biopsy in Melanoma Delays Recurrence but does not Change Melanoma-Related Survival – a Retrospective Analysis of 856 Patients
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The status of the sentinel node (SLN) is an important parameter to predict the prognosis of melanoma patients but it is a matter of debate if removal of micrometastases by SLN biopsy (SLNB) influences the prognosis of melanoma patients. We sought to investigate the impact of SLNB in melanoma patients with regard to recurrence free survival, overall survival, and metastatic pathways. 856 melanoma patients with a primary melanoma (tumor thickness 1 mm) and without clinical evidence of metastases at time of melanoma diagnosis were retrospectively studied. In 378 patients the melanoma was removed without SLNB from January 1995 until March 2000 (preSLNB-group). In 478 patients the melanoma was removed with SLNB from April 2000 until December 2004 (SLNB-group). Otherwise, both groups received identical surgical treatment of the primary melanoma and initial staging procedures performed by the same team of physicians. Follow up recommendations were also identical in both groups. Both groups showed no significant differences with regard to Breslow thickness, Clark level, ulceration and location of primary melanomas. By Kaplan Meier analyses, melanoma related overall survival was comparable in both groups. However, recurrence free survival was increased in preSLNB patients due to significantly fewer regional lymph node metastases, whereas frequencies of loco-regional cutaneous and distant metastases were comparable in both groups. We conclude that SLNB advances the detection of regional lymph node metastases and avoids therefore nodal recurrences but does not influence metastatic behaviour of melanoma cells and does not protect patients from melanoma related death caused by distant metastases.

FC26
Isolated HMB45 or MelanA Positive Cells Are Without Prognostic Significance in Melanoma Sentinel Lymph Nodes
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Significance in Melanoma Sentinel Lymph Nodes

The detection of micrometastases (defined as groups of malignant cells) in the sentinel lymph node (SLN) is an important prognostic tool in melanoma. The use of immunohistochemistry with melanocytic markers such as HMB45 and MelanA increases the detection rate of micrometastases but there are also cases with isolated immunohistochemically positive cells (IPC). To determine the prognostic significance of isolated HMB45 and/or MelanA-positive cells in melanoma SLN, we compared 47 patients with isolated IPC to 308 patients with negative SLN and to 122 patients with micrometastases. By Kaplan Meier analyses, relapse free survival (RFS) and overall survival (OS) of patients with isolated IPC were similar to SLN negative patients, whereas patients with micrometastases had a significantly worse RFS and OS. In the 47 patients with isolated IPC, 5 relapses (10.6%) and 1 melanoma related death (2.1%) occurred, in the SLN negative patients 31 relapses (10.1%) and 16 melanoma deaths (5.2%), in the patients with micrometastases 45 relapses (36.9%) and 24 melanoma related deaths (19.7%). Prognosis of patients with isolated IPC did not correlate with number of cells, type of positive staining (HMB45, MelanA, or both), presence of cytologic atypias, or tumor penetrative depth. In conclusion, isolated IPC in melanoma sentinel lymph nodes are without prognostic significance. Sentinel lymph nodes with this finding should be reported as negative.

FC27
Lack of Survival Benefit After SLNB: Results of a Monocentric Retrospective Analysis
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Background: Sentinel lymph node biopsy (SLNB) and following lymph node dissection (SLND) is commonly performed in the treatment of primary cutaneous melanoma (CM). The role of SLND in the treatment of CM is still discussed controversially. Until now no definitive guidelines do exist. Methods: 879 patients with primary cutaneous melanoma treated in the Department of Dermatology of the University of Tübingen were analysed using Kaplan Meier analysis and Log Rank tests. 419 patients treated with SLNB/SLND from 1996 to 2000 were compared retrospectively to 440 patients with a tumor thickness of 1.00 mm or more without SLNB (control collective) concerning the metastatic course, disease free and overall survival. Results In a median follow up time of 50.2 month SLNB patients showed a significantly lower rate of primary lymph node metastases (p<0.0001) whereas no significant differences were observed for primary locoregional recurrences (p = 0.59) or distant metastases (p = 0.136). Concerning disease free survival, SLNB/SLND patients showed a longer disease free survival than patients without SLNB/SLND (p = 0.023), whereas the SLNB had no effects on the distant metastasis free survival (p = 0.75) or the overall survival (p = 0.275). Conclusion In this analysis SLNB/SLND fits the aim to restrict primary regional lymph node metastasis in the follow up and seems to have a positive effect on a prolonged disease free survival. However, no effect on the distant metastases free survival and the overall survival could be demonstrated.

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FC28
Molecular Detection of Melanoma-Associated Markers in Blood: MUC-18 Is Associated with High Grade Malignancy and Poor Prognosis

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Detection of circulating melanoma cells (CMC) in peripheral blood (PB) was first reported by Hoon D.S. et al (1995), who described the use of a multi-marker RT-PCR assay to evaluate the presence of early disease recurrence or progression. The aim of our study was to report the clinical effectiveness of cancer treatment and to detect melanoma patients by an erythematous rash. PDGF may play a role in the pathogenesis of melanoma patients with redness and in 4 of the 7 (57%) melanoma patients without redness. PDGF was positive in all 6 (100%) melanoma patients with redness and in 4 of 7 (57%) melanoma patients without redness. VEGF was positive in 3 of the 6 (50%) melanoma patients with redness and in 4 of the 7 (57%) melanoma patients without redness. Positivity of blood sharing at least 3-4 markers. We didn't detect any association of blood lacking at least 3 markers. We didn't detect any association with the expression of VEGF, MUC-18 and PDGF. MUC-18 is well-known to be a MAM associated with tumor progression. In our study, MUC-18 is the only marker associated with more advanced disease stage, both alone and in combination with the other MAMs.

FC29
Hereditary Multiple Cutaneous and Uterine Leiomyomatosis

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Hereditary multiple cutaneous and uterine leiomymasmatosis (MUCUL) is an autosomal dominant disease which can be associated with type II papillary renal cancer (HLRCC). The genetic locus for MUCUL and HLRCC was recently mapped to chromosome 1q42.3-43 and germline mutations in the fumarate hydratase (FH) gene have been found. FH is an enzyme that catalyzes the conversion of fumarate to malate in the tricarboxylic acid cycle. The FH gene seems to act as tumor suppressor since loss of the wild-type allele has been identified in cutaneous, uterine, and renal tumour of MUCUL/HLRCC patients. FH enzymatic activity is absent in mutated proteins but, since the disorder is transmitted with heterozygous modality, patients show a reduced activity near to 50%. We report a study on an Italian family with history of cutaneous leiomyomas and uterine fibroids. The first patient is a 35 year-old man affected by multiple brownish nodules localized on the abdomen with a past medical history of surgical removed cutaneous leiomyomas 15 years before. The past medical history of the patient's mother revealed a surgical hysterectomy for multiple uterine fibroids. Moreover, she also presented multiple brownish nodules on her trunk. The histopathology of the skin lesions confirmed, in both patients, the diagnosis of MUCUL. Molecular analysis on FH gene mutations is also presented.

FC30
Redness, a Possible Signpost for Malignant Melanoma

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Objective: To confirm the existence and determine the mechanism of a previously described observation of erythematous macular eruption in melanoma patients. Materials: The first study consisted of 3 groups whose clinical parameters were monitored for 12 months: 14 randomly selected melanoma patients; 15 patients with basal cell carcinoma, 10 patients with squamous cell carcinoma, and 10 patients with Bowen’s disease; and 30 healthy individuals. In the second study biopsy specimens from 13 patients with melanoma, 6 with erythematous eruptions and 7 without, were studied by immunohistochemistry for the expression of vascular endothelial growth factor (VEGF) and platelet growth factor (PDGF). Results: In the first study 8 out of 14 (57%) melanoma patients exhibited an erythematous macular rash adjacent to and in the general vicinity of the primary tumor. Neither of the other two groups displayed such a rash. In the second study VEGF was positive in 3 of the 6 (50%) melanoma patients with redness and in 4 of the 7 (57%) melanoma patients without redness. PDGF was positive in all 6 (100%) melanoma patients with redness and in 4 of the 7 (57%) melanoma patients without redness. Conclusion: Melanoma development and progression is accompanied in some patients by an erythematous rash. PDGF may play a role in the pathogenesis of the redness by affecting the vasculature function rather than abundance. The significance of this observation for detection, treatment, and prognosis of malignant melanoma will be discussed.

FC31
Metastatic Subcutaneous Liposarcoma

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We present a case of a 51-year-old patient, admitted to our department for the complaint of a firm, red-brownish, partially ulcerated plaque on the left gluteal region. The lesion measured about 5 cm in diameter. In 2002 the patient had undergone surgical excision of a subcutaneous liposarcoma on the left knee and had then received postoperative radiation. Besides malignant fibrous histiocytoma, liposarcoma is the most common malignancy arising from soft tissues in adults. It represents 20% of all mesenchymal tumors. It is usually located on the lower extremities and it is mostly intramuscular whereas the subcutaneous forms are quite rare. In 30% of the cases liposarcoma disseminates to other organs and mortality is about 40%. Recurrence and metastatic rates are very different, according to the various subtypes of liposarcoma. The World Health Organization has classified liposarcoma in five histologic categories: well differentiated, mixoid, round cell, pleomorphic and dedifferentiated. The better prognosis is associated to well-differentiated and mixoid subtypes. Primitive subcutaneous liposarcoma is very rare, mixoid and well-differentiated liposarcomas are the most common subtypes.
FC32
Multimarker Real-Time RT-PCR for Quantitative Detection of Melanoma Associated Antigens, a New Approach
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Interferon-alpha is a standard treatment in patients with malignant melanoma belonging to stage II and III. However, it is essential to be able to detect the therapeutic response of adjuvant immunotherapy and to investigate if the disease is showing regression or progression in clinically tumor-free patients. The best candidate for such examination seems to be the quantitative detection of tumor associated antigens. In the past, different authors discussed the relevance of such detection due to the result inconsistency. However, the main problem was a methodological difference among various studies. The majority of the previous studies has been carried out with a single marker, detected by conventional or semiquantitative RT-PCR. In our study, we introduced a quantitative multimarker real-time RT-PCR. This method detects the expression of tyrosinase, MART-1, MIA, MAGE-3 and gp 100 genes exhibiting high specificity for melanoma cells. Fifty melanoma patients at stage II and III were regularly examined within one year. In our preliminary results, down-regulation of different markers after the onset of the immunotherapy with interferon-alpha was observed. Furthermore, a strong correlation between the up-regulation of different melanoma-associated marker expression level and development of distant metastases was seen. The best candidate for this purpose seems to be MAGE-3 which became positive in 85% of examined patients developing distant metastasis. The results provide us with information on the frequency of melanoma-associated gene transcripts and help us to determine which patients are at risk of developing distant metastases and how we should proceed with the immunotherapy. The final aim of our study is the routine usage of this method for rapid screening in risk patients. The work was supported by the MOH IGA 1A 8243-3 Grant.

FC33
Giant Pilomatrixoma
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Pilomatrixoma is a benign skin neoplasm of hair matrix origin that may occur at any age although it is most common in childhood, adolescence and in adults over 60 years of age. Clinically, pilomatrixoma typically presents as a solitary, asymptomatic, firm, skin-colored to faint blue/red nodule located on the head and neck. The average size is 1 cm and it very rarely exceeds 3 cm in diameter. Uncommon clinico-pathologic variants of pilomatrixoma such as giant, bullous-like, anetodermic, exophytic, perforating/ulcerated and lymphangiectatic lesions have been rarely described. We report a 52-year-old man who was examined for an ulcerated, reddish nodule measuring 11 x 6 x 5.5 cm, located on the left clavicular region. The lesion had been present for approximately 7 years; it had rapidly increased in size and ulcerated during the last 2 months. The patient complained occasional burning and pain. Clinical differential diagnoses included cutaneous lymphoma, sarcoma, squamous cell carcinoma and cutaneous metastasis. Histopathologic examination revealed a circumscribed large tumor involving the whole dermis and the subcutis, composed of partially confluent foci of aggregations of matrical cells admixed with eosinophilic cornified material containing shadows cells. In addition, multinucleated giant cells, areas of calcification and metaplastic ossification, edema and hemorrhage were also observed. Based on the clinico-pathologic features the diagnosis of giant pilomatrixoma was made. In conclusion, giant pilomatrixoma can be included in the spectrum of benign giant adnexal neoplasms.

FC34
Cutaneous Photochemoprotection With Topical Application of Low Dose Green Tea Extract (OM24®) in Humans – a Placebo-Controlled Trial
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Background: Prerclinically, green tea extracts (GTEs) have shown reduction of UVB-induced (i) erythema, (ii) DNA damage, (iii) formation of radical oxygen species and (iv) upregulation of numerous factors related to apoptosis, inflammation, differentiation and carcinogenesis. In humans, topical GTEs have only been tested in limited studies, with very high concentrations and over short periods of time. Here, the utility of topical GTEs as everyday photoprotective agents was tested. Proband and Methods: 18 Probanda applied over 34 days on UV-protected skin verum (= W/O cream with 0.4% GTE, OM24®) and placebo. 24 h after irradiation with 100mJ/cm2 UVB, biopsies were taken on day 6 and 34: (A) non-irradiated; (B) placebo + UVB; (C) GTE + UVB. On paraffin sections, thymidine dimers, p53, and apoptosis (sunnburn cells and TUNEL assay) were histochemically assessed. Preliminary results: Tolerability was excellent. Comparing biopsy C with B, p53-positive keratinocytes were reduced in C, by 31.9% (p = 0.002) on day 6 and by 36.3% (p = 0.001) on day 34. As was apoptosis [TUNEL-Asay, 66.3% reduction (p = 0.027) on day 6; and 38.5% reduction (p = 0.097) on day 34; sunburn cells, 38.9% reduction (p = 0.02) on day 6]. Thymidine dimer-positive keratinocytes and erythema response were unchanged between biopsies C and B. Conclusions: Already at low, cosmetically usable, non-erythema-reducing concentrations (0.4%), topicaly applied GTE (OM24®) significantly reduces UVB-mediated induction of p53 and apoptosis without tachyphylaxis over five weeks, suggesting GTEs as suitable everyday photoprotective agents.

FC35
Clinical Benefits of Imiquimod 5% Cream Applied Once Daily 3 Days per Week for the Treatment of Actinic Keratoses in Immunosuppressed Organ Transplant Recipients
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Introduction: Non-melanoma skin cancer represents a significant cause of morbidity in organ transplant patients. In grafted patients the relative risk of invasive squamous cell carcinoma and actinic keratoses (AK) is up to 250 times higher compared to non-immunocompromised patients. Topically applied, imiquimod 5% cream induces local interferon-alpha, interleukin-12 and tumor necrosis factor alpha. Imiquimod has the potential to be an effective option for the treatment of AK in organ transplant recipients. Methods: A randomized, double-blind study evaluated 43 solid organ transplant recipients with multiple AKs (4 to 10 lesions). The patients applied imiquimod or vehicle cream to AK lesions in a 100 cm2 area once daily 3 times a week for a period of 16 weeks. This study compared imiquimod 5% cream and vehicle cream with respect to graft-safety and efficacy (complete and partial clearance rates). A posttreatment biopsy of a marker lesion was performed at the end of study. Results: Of the subjects randomized to imiquimod, overall clinical/histological clearance rate was 62.1% (18/29); and 0.0% (0/14) for vehicle subjects. No graft rejections or trends for a deterioration of the graft function were detected. Local skin reactions were well tolerated. Preliminary Conclusion: The results of this study demonstrated that topical imiquimod provides a clear medical benefit in the treatment for multiple AK lesions located in large treatment fields in high risk solid-organ transplant patients.