ABSTRACTS

FC16
Topical Corticosteroids in Early Mycosis Fungoides: When and How?
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The treatment options for early mycosis fungoides (MF) should not be outside the field of skin-directed therapies. In stage IA, and at a lesser extent in patch stage IB MF, class I topical corticosteroids (TCs) – mostly clobetasol propionate – can be an effective first-line treatment. Recent data showed an overall response of 94% (63% CR) in stage IA MF patients. These data are worth of attention, even though long term follow-up data are not available to date. In addition to the above, the possible use of TCs in early MF or in later stage MF patients relapsing with few patches can be considered as an integration to other treatment modalities (PUVA, narrow-band UVB, topical chemotherapy). In this latter case, the clinical practice also suggest the possible use of class II TCs, with a much lower risk of local and systemic side effects. This is especially worth of consideration taking into account the higher susceptibility to side effects of pretreated MF patients.

FC17
Possible Involvement of Borrelia Burgdorferi and HCV in the Aethiology of Mycosis Fungoides
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Mycosis fungoides is the most frequent cutaneous T-cell lymphoma with an unknown etiology. Several aethiopathogenetic mechanisms have been postulated, including persistent viral or bacterial infections. We looked for the presence of Borrelia burgdorferi, an aethiologic agent of Lyme disease and Hepatitis C virus (HCV) in a case study of mycosis fungoides patients from Northeastern Italy. Polymerase chain reaction was used to detect Borrelia burgdorferi genome, while RT-PCR was performed for HCV analysis. The case study was composed of formalin-fixed and paraffin-embedded lesional skin biopsies of 83 patients with mycosis fungoides and 83 sex- and age-matched healthy controls with homo-localized cutaneous nevi. Borrelia burgdorferi-specific sequence was detected in 15 out of 83 skin samples of patients with mycosis fungoides (18.1%), but in none out of 83 matched healthy controls (p < 0.0001). Positivity for HCV was detected in 4 out of 83 MF samples and in 3 out of 83 controls (p = 0.279). This study shows no association between MF and HCV infection. Borrelia burgdorferi positivity rates detected in this study support a possible role of Borrelia burgdorferi in the aethiopathogenesis of mycosis fungoides in the population endemic for Lyme disease.

FC18
Measles Virus Oncolytic Activity in Cutaneous T-Cell Lymphoma – In Vitro and In Vivo
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Measles virus has shown promise as an oncolytic virus in the treatment of different tumor models for human B-cell lymphoma, multiple myeloma, ovarian cancer, and glioma. In human cutaneous T-cell lymphoma (CTCLs) deficiency of neoplastic T-lymphocytes in interferon signaling has been shown, thus rendering them susceptible for viral oncolysis. We evaluated cytopathic effects of measles virus (MV) in human CTCL cell lines in vitro and in vivo in a mouse tumor model of human CTCL. CTCL cell lines originating from patients expressed MV receptors in human CTCL cell lines in vitro and in vivo in a mouse tumor model of human CTCL. CTCL cell lines originating from patients expressed MV receptors CD150 and CD46 and were easily infected by MV, resulting in oncolysis in two cell lines and slow reduction in viability of the third. CTCL tumors established from one of these CTCL cell lines (MyLa) in nude mice with treated with recombinant MV. Intratumoral treatment led to complete tumor regression in treated mice, while control mice showed exponential tumor growth. Immunohistochemical analysis of biopsies during intratumoral treatment with MV revealed local viral activity with positive staining for MV NP protein. The data demonstrate the inherent potential of MV as a therapeutic agent against CTCL with potential application in clinic.

FC19
Primary Cutaneous T-Cell Anaplastic Large Cell Lymphoma CD30+ in a Heart Transplant Patient: Report of a Case and Literature Review
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Solid organ transplant recipients are more at risk of developing a wide range of malignancies including skin tumours and lymphoproliferative disorders. The risk of post-transplant lymphoproliferative disorder (PTLD) is 28-49 times the risk of lymphoproliferative disorder in the normal population. Most cases are of B-cell phenotype and are associated with Epstein-Barr virus (EBV) infection. PTLD presenting clinically in the skin are rare and usually of B-cell phenotype. Only rare cases of cutaneous T-cell PTLD have been previously reported, mostly mycosis fungoides type. We describe a rare primary cutaneous T-cell lymphoma CD30+ arising in a heart transplant patient who developed a solitary nodule on his right leg 12 years following heart transplantation. An excisional biopsy was performed and the morphology and the immunohistochemical findings were consistent with a CD30+ anaplastic large cell lymphoma with a T-cell phenotype. There was no clinical evidence of systemic spread of the lymphoma. After the histological diagnosis, radiotherapy in correspondence of the affected area was performed. In our patient no further lesions appeared within 9 months. Knowledge of this rare T-cell PTLD is limited, although from the review of the literature it seems that this disorder has a propensity for a more aggressive course in immunosuppressed patients.
FC20
CD56 Lymphoproliferative Disorders of the Skin: A Multicenter Study from the European Organization for Research and Treatment for Cancer (EORTC) Cutaneous Lymphoma Project Group

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Cutaneous lymphomas expressing CD56, a neural cell adhesion molecule, are characterized by a highly aggressive clinical course and a poor prognosis. However, prognostic subsets within the CD56+ group have been difficult to identify due to lack of uniform clinicopathological and immunophenotypical criteria. To define prognostic parameters and guidelines for diagnosis and treatment for CD56+ hematological neoplasms presenting primarily in the skin a multicenter study was conducted by the cutaneous lymphoma task force of the EORTC. As a result four different subtypes of lymphoproliferations with CD56 expression could be identified: 1) hematodermic neoplasm, 2) skin infiltration as first manifestation of CD56+ acute myeloid leukemias, 3) extranodal NK/T-cell lymphoma, nasal type and, 4) “classical” cases of cutaneous T-cell lymphoma (CTCL) with co-expression of the CD56 molecule. Patients of the first three groups had a poor outcome (93% died) with a median survival rate of 11 months (confidence interval 2–72 months), whereas all patients of the last group were alive at the last follow-up. Our findings indicate that CD56+ cutaneous lymphoproliferative disorders presenting in the skin have a poor prognosis. However, “classical CTCL” cases can show co-expression of this molecule, which does not affect the indolent clinical course. These cases should not be mistaken as CD56+ aggressive neoplasms and therefore aggressive treatment should be avoided.

FC21
Photodynamic Therapy with Methyl Aminolevulinate as a Valuable Treatment Option for Unilesional Cutaneous T Cell Lymphoma

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Background: Mycosis fungoides (MF) is the most common primary Cutaneous T cell Lymphoma (CTCL). Unilesional MF is characterized by a limited involvement of the skin and a chronic though indolent course. If lesions are refractory to topical steroids, therapies such as localized chemotherapy, photochemotherapy and radiotherapy are available. However, they have several acute and chronic side-effects and toxicity may accumulate if repeated and protracted treatment cycles are delivered to refractory or relapsing lesions. The present study aims to assess the efficacy of photodynamic therapy (PDT) with topical methyl-aminolevulinate (MAL) in the treatment of unilesional MF. Methods: Five patients were enrolled who were suffering from unilesional MF which did not respond to treatment with topical steroids, localized PUVA or UVA1 phototherapies. A 20% MAL (Methvix cream®), Galderma, F) cream was applied under occlusive dressing for 3 hours. Soon afterwards, skin was irradiated with 37.5 J/cm2 of red light (635 ± 18 nm) delivered by an Aktilite CL128 lamp (PhotoCure ASA, Oslo, Norway) with an irradiance of 86 W/cm2 at skin level. PDT was repeated once weekly until complete clearing of the lesions was obtained, or, in the case of partial clearing, the therapy was interrupted when 3 successive treatments provided no further improvement. All patients underwent a skin biopsy before and after PDT. Results: A complete remission was observed in 4 patients and a partial improvement in 1. The median number of treatments was 6 (range 1-9). In no cases was recurrence seen at follow-up (ranging from 12 to 34 months). Treatments were well tolerated and local anesthesia was never requested. Conclusion: In conclusion, PDT was here seen to be an effective and well tolerated treatment option for unilesional MF.

FC22
Methyl Aminolevulinate Photodynamic Therapy (MAL-PDT) for the Treatment of Early Stage Mycosis Fungoides

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Therapy for mycosis fungoides (MF) is based on clinical stage. Although treatments for early or localized patch stage MF may appear to result in cure, the practical aim is to achieve and maintain clinical remission, decrease morbidity, and palliate advanced disease. Multiple therapeutic modalities exist, from topical therapy, phototherapy, photopheresis, radiation therapy, immunotherapy, chemotherapy, or newer agents such as anti-tumor vaccines and antibody fusion toxins. Photodynamic therapy (PDT) is a developing approach to the treatment of cancer and other diseases that involves the use of light to activate photosensitizer molecules. Topical agents such as methyl aminolevulinate (MAL) may be used for the PDT, as it acts as powerful photosensitizer. Isolated reports of efficacy were reported for treating cutaneous T-cell lymphomas. It has been shown that PDT inhibits the proliferation of malignant lymphocytes. Here we report the use of MAL-PDT in 4 patients affected by MF (Stage Ia, Ib, Ila) and treated with MAL cream (160 mg/g) and 75 J/cm2 red light (570-670 nm) and the number of repetitions were individually chosen in reaction to the individual tolerability and clinical outcome. Adverse events, such as erythema, edema and crust formation, were mild to moderate, and treatment was well tolerated. The results are discussed. In our preliminary experience MAL-PDT led to partial remission in localized lesions and further investigation regarding its role as a possible useful addition to standard therapies is needed. Further studies are necessary in order to determine the optimal light dose and treatment interval.

FC23
Final Results of a Phase I/II Multicentric Trial of Adenovirus-Interferon-γ (TG1042) Demonstrate Good Tolerance and Efficacy in Relapsing Primary Cutaneous Lymphoma (PCL)

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Background: Adenovirus (Ad) is a non-enveloped virus that can deliver genes into cells. A phase I/II trial of a non-replicating recombinant adenovirus (Ad-hIFN-γ-cDNA insert) in patients with advanced primary T cell (CTCL) or B cell (CBCL) CL. One to 3 lesions were injected on day 1, 8 and 15 with no treatment during the 4th week (a 4-week cycle) and thereafter up to 12 cycles. Immunohistochemistry and quantitative PCR were performed on injected lesions biopsied at baseline and after the 1st cycle. In the phase I, 18 patients were enrolled in 3 successive cohorts at the doses of 3x109 viral particles (vp) (n = 3), 3x1010 vp (n = 3) and 3x1011 vp (n = 12). In the phase II, 21 patients have been treated at 3x1011 vp. To date, enrolment is completed, 39 patients (32 CTCL and 7 CBCL) have been included, 3 of them are still on treatment. Injection site reaction and flu like syndrome and fatigue were the most common adverse events. Transgene-hIFN-γ mRNA was detected in injected lesions. Gene expression analysis of biopsies and PBMC showed up-regulation of hIFN-γ inducible genes. Local clinical response has been observed in 17 (including 9 complete responses) out of 31 evaluable patients. Thirteen global responses (7 CR, 6 PR) out of 30 evaluable patients have been observed. All 5 evaluable CBCL responded (3 CR). These results demonstrate that TG1042 is well tolerated and presents a potential significant benefit for the treatment of both CTCL and CBCL.