019 Herpes simplex virus infection in pemphigus patients: a prospective study

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This study aims to consider herpes simplex virus (HSV) infection in front of any severe, recalcitrant lesions and to remove any unexplained test with a high outcome. Prospective study over 15 months (September 2019 - November 2020), 8 cases of PV associated with HSV infection were collected. 1 case of seseobion, 3 cases of folliculitis, 4 cases of cutaneous. PFAI score ranged between 23-102. Sex ratio 1.47 - 1, median age 46.5 years. The mean duration of PV was 5.5 months (2 patients were hospitalized for relapses and 6 had PV de novo). PV was confirmed on skin biopsy, direct and indirect immunofluorescence. The treatment was based on oralmined agents and aciclovir. While recently JAK inhibitors are used off-label, despite the possible long-term effect associated to their broad immunosuppressive activities, the combination of steroid and minoxidil is still considered to be an effective treatment for AA with fewer side-effects, we investigated the potential of TAG-0003 as an AA treatment.

021 A retrospective analysis of the clinical, biochemical, immunological, histopathological and radiological spectrum of Systemic Lupus Erythematosus at a tertiary care centre in North India

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The objective of our study was to retrospectively analyse the clinical, biochemical, immunological, histopathological, and radiological spectrum of Systemic Lupus Erythematosus (SLE) in North India. We retrospectively analysed the medical records of all patients who presented with SLE to a tertiary care centre in North India from January 2011 to August 2021. We included only records of patients with detailed information on history, examination, biochemical, immunological, histopathological and radiological investigations. We analysed the medical records of 145 patients (89 (61.6%) females and 56 (38.4%) males). The age of the patients ranged from 13-81 years. Seventy-four (82%) patients were females and the rest were male. Most of the patients presented with fever, joint pain and photosensitivity. Nearly all patients had lesions suggestive of cutaneous lupus erythematosus. Thirty-two (65%) patients underwent pleural effusion, and three had pleural effusion. One patient had antibodies to lupus anticoagulant. Twelve patients had low C3 levels, and seven patients had low C4 levels. This retrospective analysis presents an insight into the manifestations of systemic lupus erythematosus in North India and sheds light on the disease status and treatment response.

022 Exploring the potential of the novel IFN-α receptor antagonist TAGCX-0003 as a treatment for alopecia areata in pre-clinical models

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Alopecia areata (AA) is an autoimmune hair loss disorder in which hair follicles (HF) that have lost their protective immune privilege (IP) are attacked by an inflammatory cell infiltrate including key effector CD8+ and NG2+ cells rapidly turn into catagen. IFN-α is recognized as a key pathogenic cytokine in driving IP collapse and AA pathogenesis. While recently JAK inhibitors are used off-label, despite the possible long-term effect associated to their broad immunosuppressive activities, the combination of steroid and minoxidil is still considered to be an effective treatment for AA. Given that the selective inhibition of IFN-α could provide an effective treatment for AA with fewer side-effects, we investigated the potential of TACGysz’s proprietary sDNA IFN-α receptor antagonist TAGCX-0003, characterized by high affinity against IFN-α (Kd=33pM) in pre-clinical human models. Systemic administration of 0.3 and 3.0mg/kg TAGCX-0003 significantly suppressed IFN-α induced premature catagen development and blocked MHC class I and II up-regulation in the hair bulb. Since the main target in human scalp skin is to treat the hair bulb, we investigated the effects of TAGCX-0003 in vitro. After treatment with 0.3mg/kg TAGCX-0003 for 24 hours, in 1 hour of treatment, we observed inhibition of the hair bulb. Intra-dermal administration of TAGCX-0003 (12-30nm) promoted hair growth in rodent models, in which AA-like phenotype was induced by injection of CD8+ and NG2+ cells, similar to steroid-induced AA-like phenotype in humans. TAGCX-0003 was well tolerated, along with decreased numbers of CD8+ T-cells in and around the bulb. However, only TAGCX-0003 significantly reduced MHC I and II expression in around hair bulbs, thus rescuing HF from IP collapse. Taken together, our pilot data reveal that IFN-α neutralization restores HF IP collapse, potentially preventing disease relapse, and support the further exploration of TAGCX-0003 as an AA treatment.

023 RNA sequencing of chronic GVHD skin lesions identifies TREM1 as a possible therapeutic target in lichen planus

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Cutaneous involvement of chronic graft-versus-host disease (cGVHD) has a wide range of manifestations including a lichenoid form with a currently assumed mixed Th1/Th2 signature and a sclerotic form with Th1 signature. Despite substantial heterogeneity of innate and adaptive immune cells recruited to the skin and of the different clinical manifestations, treatment depends mainly on the severity of the skin involvement, and relies on systemic high-dose glucocorticoids. We performed the first study using RNA-Seq to profile and compare transcripts of lichen planus (LP) and chronic GVHD (cGVHD) (n=6) to control skin and healthy controls (CONT, n=6). We identified 2945 DEG when comparing LP to CONT, and 1652 when comparing morphea to CONT. 979 DEG were shared between the 2 subtypes (e.g., CC29, CCL10, CCL11). GSEA identified 2 gene sets enriched in both subtypes that are related to IFN-γ and IL-17 responses. Using IPA we identified “IFN signaling” as the most important canonical pathway predicted to be activated. 208 DEGs were identified when comparing LP to morphea. Among the most significant canonical pathways, triggering receptor expressed on myeloid cells 1 (TREM1) signaling pathway was predicted to be activated. TREM1 is a cell surface receptor mainly expressed on myeloid cells, known to amplify an inflammatory response. In conclusion, we unravelled common and unique inflammatory pathways in cGVHD, including IFN-signaling pathway that seems to play an important role in both chronic planus and morphea cGVHD, as well as the TREM1 signaling pathway that could be a promising therapeutic target in LP cGVHD.

024 Comparative analysis of ex vivo assays aimed at identifying Desmoglein 3 reactive CD4+ T cells in pemphigus vulgaris

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1 Department of Dermatology and Allergology, Philippus-Universität Marburg, Marburg, Germany, 2 Marburg, Germany, 3 Autoimmune reactive CD4+ T cells against the desmosomal protein, Desmoglein 3 (Dsg3), play a central role in the pathogenesis of pemphigus vulgaris (PV). Accordingly, descriptive and functional analyses of these cells ex vivo are of great interest. Here, we investigated the phenotype and pathogenicity of CD4+ T cells within PV patients. Flow cytometric analysis enabled phenotyping of CD4+ T cells and even identification of Dsg3-reactive CD4+ T cells by using fluorochrome-labeled HLA-DPB1*02:04:02 multimers loaded with immunogenic Dsg3 peptides. Proliferation of CD3+CD4+ T cells was studied by CFSE-dye dilution in response to in vitro stimulation with Dsg3 or Dsg1 peptides. ELISPOT analysis characterized cytokine-secretion profiles of CD4+ T cells in response to Dsg3-stimulation. In contrast to healthy controls, PV patients showed an increased number of activated CD4+ T cells with a stimulatory capacity. Dsg1-reactive CD4+ T cells proliferated in response to specific Dsg1 peptides and especially IL-5 secretion was enhanced in PV patients. In conclusion, our data highlight the importance of CD4+ T cells contributing to PV pathogenesis and thus serve as basis for the development of targeted therapy in the future.