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The development of a disease-specific quality of life instrument for autoimmune Bullous diseases - The ABQOL
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A phase 2, open-label, Investigator-initiated study to evaluate the safety and efficacy of Apremilast in subjects with recalcitrant contact or Atopic dermatitis

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Atopic dermatitis (AD) and allergic contact dermatitis (ACD) are chronic inflammatory diseases characterized by pruritus and erythematous plaques that become lichenified over time. Current systemic treatments are associated with numerous end-organ toxicities. Apremilast is a novel phosphodiesterase type IV inhibitor which has been shown to decrease TNF-α, IFN-γ, IL-2, IL-8, IL-12, IL-17, IL-20, IL-23, leukotrienes, and NO in human cell lines. Phase 2 studies demonstrated efficacy in patients with psoriasis or psoriatic arthritis. This therapy may offer improved control over AD and ACD. The primary objective is to evaluate the efficacy and safety of Apremilast in patients with recalcitrant moderate to severe atopic or contact dermatitis. This study is a proof-of-concept, phase 2, open-label, single institution trial to evaluate the efficacy, safety, and tolerability of Apremilast, 20 mg capsule twice daily for twelve weeks, in ten subjects. Clinical efficacy was determined by the Eczema Area and Severity Index (EASI) and the Investigator Global Assessment (IGA). Preliminary results show that half of the patients experienced a 10% or greater improvement in EASI scores during the treatment phase. Half of the subjects also demonstrated a one-point improvement in IGA from baseline. Overall, there was a 5% worsening in mean EASI scores in all eight subjects. In two subjects who completed treatment, one experienced a 32% improvement in EASI score and a one-point improvement in IGA. Two patients in treatment phase experienced a 46% and 56% improvement in EASI at week 8 and week 10, respectively. Both patients had a one-point improvement in IGA. The two patients who withdrew consent had a 10% and 20% worsening in EASI with no change in IGA at week 2. All patients tolerated Apremilast well with no serious adverse events or withdrawal due to side effects. Common side effects included headache, dermatitis flare, and mild GI distress (nausea, dysgeusia, soft stool). Small study with low power. Small arm with no control. Early results of this ongoing trial demonstrate that Apremilast is well-tolerated in subjects with 50% showing mild improvement in their dermatitis during the 12-week treatment course. However, the efficacy was modest and not as good as that seen in patients with moderate to severe psoriasis.

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Ctotoxic chemotherapy for metastatic widespread cutaneous T-cell lymphoma (CTCL) in response to systemic chemotherapy is a common challenge. Apremilast is an oral phosphodiesterase type 4 inhibitor that targets the downstream signaling of various cytokines involved in the pathogenesis of CTCL. Apremilast has demonstrated efficacy in patients with psoriasis or psoriatic arthritis. This therapy may offer improved control over AD and ACD. The primary objective is to evaluate the efficacy and safety of Apremilast in patients with recalcitrant moderate to severe atopic or contact dermatitis. This study is a proof-of-concept, phase 2, open-label, single institution trial to evaluate the efficacy, safety, and tolerability of Apremilast, 20 mg capsule twice daily for twelve weeks, in ten subjects. Clinical efficacy was determined by the Eczema Area and Severity Index (EASI) and the Investigator Global Assessment (IGA). Preliminary results show that half of the patients experienced a 10% or greater improvement in EASI scores during the treatment phase. Half of the subjects also demonstrated a one-point improvement in IGA from baseline. Overall, there was a 5% worsening in mean EASI scores in all eight subjects. In two subjects who completed treatment, one experienced a 32% improvement in EASI score and a one-point improvement in IGA. Two patients in treatment phase experienced a 46% and 56% improvement in EASI at week 8 and week 10, respectively. Both patients had a one-point improvement in IGA. The two patients who withdrew consent had a 10% and 20% worsening in EASI with no change in IGA at week 2. All patients tolerated Apremilast well with no serious adverse events or withdrawal due to side effects. Common side effects included headache, dermatitis flare, and mild GI distress (nausea, dysgeusia, soft stool). Small study with low power. Small arm with no control. Early results of this ongoing trial demonstrate that Apremilast is well-tolerated in subjects with 50% showing mild improvement in their dermatitis during the 12-week treatment course. However, the efficacy was modest and not as good as that seen in patients with moderate to severe psoriasis.

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Revisiting low dose total skin electron beam therapy in the management of Mycosis fungoides

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Total skin electron beam therapy (TSEBT) is a highly effective treatment for Mycosis fungoides (MF). The standard course consists of 36 Gy delivered over an 8-10 week period. This regimen is time intensive and associated with significant treatment related toxicities including erythema, desquamation, alopecia, edema, and chronic xerosis. The aim of this study is to perform a retrospective review of patients receiving low dose TSEBT in an attempt to identify a lower dose alternative while retaining a favorable efficacy profile. We identified 102 patients with mycosis fungoides (MF). The standard course consists of 36 Gy delivered over an 8–10 week period. This regimen is highly effective and has been shown to increase collagen VII expression in unblistered skin of RDEB-GS patients even across all three radiation subgroups (5–25 Gy). We identified 102 patients with mycosis fungoides who received low dose TSEBT (5-25 Gy) at the Department of Radiation Oncology from 1958 to 1995. Only patients with T2-T4 MF receiving a first dose of TSEBT were included. Those patients who received low dose TSEBT (5–25 Gy) at the Department of Radiation Oncology, Stanford University School of Medicine, Stanford, CA.

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Investigation of cell therapy for generalized severe recessive dystrophic Epidermolysis bullosa by intradermal allogeneic fibroblast injections randomized against placebo injections

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This is the first double blind placebo-controlled randomized controlled trial of intradermal cultured allogeneic fibroblast injections compared with intradermal injections of placebo transport solution alone in severe generalised RDEB. Intra-dermal injection of cultured fibroblasts has been shown to increase collagen VII expression in unblistered skin of RDEB-GS patients even at 3 months, yet the cultured fibroblasts had disappeared by 2 weeks (1). We designed a single institution, double blinded, intra-patient, placebo-controlled randomized controlled trial to determine the clinical response of intradermal cultured allogeneic fibroblast injections from a healthy male donor, in chronic erosions of patients with RDEB-GS and compare this with transport solution alone. Five patients each with up to 6 pairs of symmetrical wounds were biopsied and randomly injected at baseline with the two treatment arms and monitored over 12 months. Subject and Investigator Visual Analogue Scores (VAS) for appearance, pain, and pruritus, Quality of Life in Epidermolysis Bullosa (QOLIB) (2) and non-invasive testing of epidermal fluid content studies were performed. Skin biopsies were performed to determine type-VII collagen expression, electron microscopy ultrastructure, presence of inflammatory markers and fluorescent in situ hybridization (FISH). Indirect immunofluorescence for anti-type VII collagen antibodies, HLA typing and reverse transcriptase polymerase chain reaction (RT-PCR) to detect COL7A1 expression were performed. We will present the 12 month clinical and histopathological results for 5 patients. The methods used provide a feasible new therapy for RDEB patients.

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ABSTRACTS
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The development of a disease-specific quality of life instrument for autoimmune Bullous diseases - The ABQOL
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The literature puts forward that disease-specific instruments are the most specific tools available in this domain, as they are most sensitive to changes in disease status. At present, no disease-specific instrument exists for use in autoimmune bullous disease (ABD). Non-structured interviews and focus groups were conducted with 26 patients suffering ABD for item generation and validation. Eighty-eight items were combined and reduced to form a pilot QOL in autoimmune bullous disease (ABQOL) questionnaire with 45 questions, which was distributed to 73 ABD patients across Australia, along with the Dermatology Life Quality Index (DLQI). Bullous experts were then consulted in an attempt to further refine the 45-questions before factor analysis was completed. Statistical analysis was then performed to assess the utility of the pilot ABQOL. Item performance features such as item difficulty, response distribution, item-test and item-rest correlation were performed on each question after first stratifying each item under three subscales—‘symptom’, ‘function’ or ‘emotion’. Content validity and discriminant validity were also assessed and test-retest studies were also conducted. Internal consistency was assessed by calculating Cronbach alpha values for each subscale. Face and content validity were established by conducting in-depth, open interviews with bullous patients as well as through review of the pilot ABQOL questionnaire by experts in bullous disease. Discriminative validity has been assessed qualitatively by reviewing the number of insensitive items in the pilot ABQOL and comparing them to the DLQI (8/10 [80%]), through which the pilot ABQOL was found to be superior to the DLQI. No items were considered difficult, and response distribution was considered optimal for most questions. Cronbach alpha coefficients were found to be above 0.70 for each of the three subscales, and thus questionnaire reliability was considered optimal. Further work is being done to refine the number of questions in the ABQOL-questionnaire. A condensed version of the ABQOL will be ready by March.

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Quality of life in Cutaneous Lupus Erythematosus
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The purpose of this study was to assess the relationship between CLE and quality of life (QOL). We specifically sought to compare QOL in CLE to other diseases and to determine which independent variables are associated with poor QOL. All patients with CLE or SLE were invited to participate in the study. Subjects were asked to complete the Skindex-29, which assesses QOL in terms of symptoms, emotions, and functioning, with higher scores indicating worse QOL. Disease severity was assessed with the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI). Mean Skindex-29 scores in CLE were compared to norms for other diseases. Mean scores within the CLE population were compared between different genders, ethnicities, and disease subtypes. Pearson’s correlation coefficients were calculated for Skindex-29 scores and disease severity, age, and age at diagnosis. 157 subjects were included in the analysis. Overall, patients with lupus were most affected in the emotions domain (m = 48, SD = 28) relative to symptoms (m = 40, SD = 23 and functioning (m = 28, SD = 25). The subscales were highly intercorrelated, such that a high score in one tended to be associated with high scores in the others (Pearson’s r range 0.65–0.78, all P < 0.0001). In the emotions domain, lupus was comparable to dermatomyositis (mean = 45, SD = 27) and vulvodynia (m = 50, SD = 20), and the other diseases were all less affected (all P < 0.0009). For functioning, only patients with vulvodynia (m = 44, SD = 22) were more impaired than patients with lupus (P < 0.0001). Female gender was associated with poor quality of life in all three domains (all P < 0.0006). There was a correlation between increased disease severity and worse QOL across all three subscales (Pearson’s r range 0.27–0.38, all P < 0.0006). There was a small correlation between younger age and worse symptoms and emotions scores (all P < 0.04). There was also a small correlation between younger age at diagnosis and worse symptoms scores (P = 0.04). CLE has a profoundly negative impact on QOL, particularly in women and individuals with severe disease.