Associations between nephritis and differential proportions of each reference cell methylome were tested using a Mann Whitney test.

Results Participant demographics by cohort (USA=6, Nigeria=8) and clinical features are shown in **table 1**. In the NYU cohort (and HC), 3 participants were Hispanic, 2 were Asian, and 3 were AA. LN was present in 50% and 62% of the NYU and Nigerian cohorts respectively. At least 100ng of DNA was extracted from 13/16 samples. Fresh, frozen, and shipped-frozen samples produced similar quality DNA; beta distributions and probe intensities were sufficient for CpG calling. PCA analysis of the top 1000 differentially methylated CpG sites revealed clusters by ancestry. Cell type deconvolution revealed that bladder, neutrophils, kidney epithelial, monocytes, CD4 T cells, CD8T Cells, erythrocyte progenitors, B cells, and NK cells were among the most highly represented. A dendrogram of cell type reference fractions produced two major clusters (C1 and C2) which differentiated LN from non-nephritis with 6/7 in C1 and 2/7 in C2 having LN (OR: 12.5, p=0.06; figure 1). In C2, one LN participant was in complete remission, and the other had predominantly proteinuric disease without active sediment. LN samples were characterized by higher relative fractions of neutrophils and monocytes, and lower fractions of CD4T cells and NK cells compared to non-nephritis samples (figure 2).

Conclusions Reached These preliminary data support the feasibility of bulk urine sediment as an epigenetic biomarker of LN, and further analysis looking at pathways and genes within cell proportions associated with LN in larger studies.

The label color indicates the presence or absence of renal disorder with green labels indicating non-nephritis and red labels indicating nephritis participants.

REFERENCES

1. Fors Nieves CE, Izmirly PM. Mortality in systemic lupus erythematosus: An updated review. *Curr Rheumatol Rep*. 2016;**18**:21
2. Feldman CH, Hiraki LT, Liu J, Fischer MA, Solomon DH, Alarcon GS, Winkelmayer WC, Costenbader KH. Epidemiology and sociodemographics of systemic lupus erythematosus and lupus nephritis among us adults with medicaid coverage, 2000–2004. *Arthritis Rheum*. 2013;**65**:753–763
3. Marumo T, Hoshino J, Kawarazaki W, Nishimoto M, Ayuzawa N, Hirohama D, Yamanouchi M, Ubara Y, Okaneya T, Fujii T, Yuki K, Atsumi Y, Sato A, Arai E, Kanai Y, Shimosawa T, Fujita T. Methylation pattern of urinary DNA as a marker of kidney function decline in diabetes. *BMJ open diabetes research & care*. 2020;**8**:1501–1501
4. Jakiela B, Kosalka J, Plutecka H, Wegrzyn AS, Bazan-Socha S, Sanak M, Musial J. Urinary cytokines and mrna expression as biomarkers of disease activity in lupus nephritis. *Lupus*. 2018;**27**:1259- 1270
5. Teschendorff AE, Breeze CE, Zheng SC, Beck S. A comparison of reference-based algorithms for correcting cell-type heterogeneity in epigenome-wide association studies. *BMC Bioinformatics*. 2017;**18**:105

401 SINGLE-CELL RNA SEQUENCING REVEALS CELLULAR DRIVERS OF UV-MEDIATED SKIN INJURY IN CUTANEOUS LUPUS

Mitra P Maz*, Feiyang Ma*, Mehrnaz Gharaee-Kermani, Amanda M Victory, Amy Hurst, Johann Gudjonsson, J Michelle Kahlenberg. *University of Michigan; Ann Arbor, MI 48109, USA*

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Background Ultraviolet light (UV) is a known trigger of cutaneous lupus erythematosus (CLE) flares in systemic lupus erythematosus (SLE) patients, yet cell populations and mechanisms driving UV- induced skin inflammation are poorly understood. In this study, we use single-cell RNA sequencing of skin from healthy control (HC) and SLE patients with a history CLE to identify differences in SLE UV responses that serve as novel mediators of UV injury.

Methods Seven HC and eight SLE patients were recruited. Biopsies were taken from the upper thigh 24 hours after treatment with 1x minimal erythema dose or from unexposed skin. Cells were processed via 10x pipelines, RNA was sequenced with an average of 10,000 reads per cell, and DEGs were analyzed and compared between HC and SLE patients.

Results Globally, an increase in type I IFN regulated gene expression was seen in SLE>HC across all cell populations after UV exposure. In the epidermis, UV exposure led to differential gene expression in basal keratinocytes (KCs) where stress responses such as S100 proteins were noted in HC, while chemokines and IFN responses were noted in SLE KC, particularly in spinous and basal inflammatory KCs. Subclustering of fibroblast (FB) populations revealed two subpopulations that increase in proportion following UV exposure in both SLE and HC, identified as IFN-FBs and IL6+ FBs. CellphoneDB analysis revealed significant crosstalk between basal inflammatory KCs and IFN- and IL6+- FBs in SLE skin, suggesting that basal inflammatory KCs represent a critical mediator of UV signal between the epidermis and dermis in lupus. Analysis of the myeloid compartment did not support an influx of pDCs into the skin at our selected timepoint. However, recruitment of myeloid dendritic cells (moDCs) was robust in both SLE and HC skin. Compared with HC skin, moDCs from SLE patients engaged in greater crosstalk with IL-6- and IFN- fibroblasts through CXCL12, a myeloid chemoattractant. Additionally, lupus moDCs engaged in crosstalk with TREM2+ macrophages, a lupus-specific skin resident population, through chemoattractant proteins as well as IL-10.

Conclusion We thus propose that in SLE skin, UV light induces unique inflammatory keratinocyte responses that educate fibroblasts and resident myeloid cells to recruit inflammatory myeloid dendritic cells, which may contribute to inflammatory cytokine production and downstream adaptive immune cell activation in SLE. Targeting of these pathways may be beneficial for prevention of photosensitive responses.

Cutaneous Lupus & Photosensitivity

402 STUDY DESIGN AND RATIONALE FOR THE EFFICACY AND SAFETY ASSESSMENT OF DAXDILIMAB, A SELECTIVE PLASMACYTOID DENDRITIC CELL DEPLETER, IN A PHASE 2 TRIAL OF PATIENTS WITH MODERATE-TO-SEVERE PRIMARY DISCOID LUPUS ERYTHEMATOSUS

Adina K Knight*, David Larson, Liangwei Wang, Linda Zhu. [1]*Horizon Therapeutics plc, Rockville, MD, USA*; **Presenting author*

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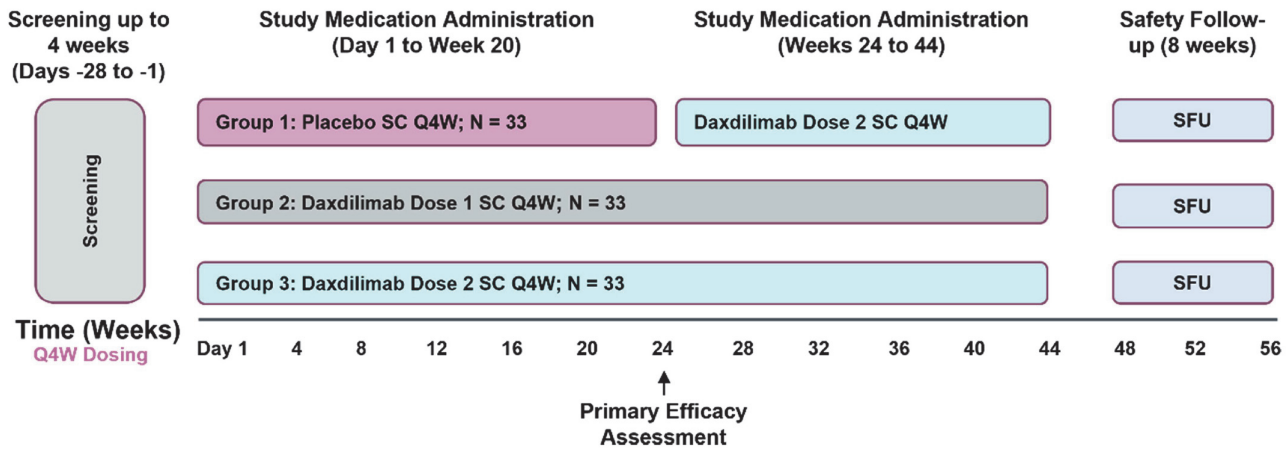
Background Daxidilimab (DAX) is an IgG1λ afucosylated monoclonal antibody specific for immunoglobulin-like transcript 7 (ILT7), a cell-surface protein that is exclusively expressed on plasmacytoid dendritic cells (pDCs). DAX binds



Abstract 402 Figure 1 Study schematic. N, total population; Q4W, once every 4 weeks; SC, subcutaneously; SFU, safety follow-up

to ILT7 on the surface of pDCs, resulting in their depletion via antibody-dependent cellular cytotoxicity. Several autoimmune disorders, including discoid lupus erythematosus (DLE), show marked enrichment of pDCs and interferon activity in affected tissue. DLE is considered the most challenging scarifying skin manifestation to treat for which a successful therapy does not currently exist.

Methods This is a 60-week Phase 2, multicenter, randomized, double-blind, placebo- controlled, parallel-group trial to investigate the efficacy and safety of DAX in reducing disease activity in adult participants with moderate-to-severe primary DLE refractory to standard of care therapy (NCT05591222, figure 1). Approximately 99 participants will be randomized in a ratio of 1:1:1 (33 participants per group) to receive subcutaneous injection of DAX arm 1, DAX arm 2, or placebo. Administration of trial intervention will occur every four weeks starting from Day 1 through Week 44. After week 24 all participants will be receiving DAX, including those assigned to the placebo arm, for the remainder of the 48-week treatment period.

Outcome Measures The primary efficacy endpoint is the mean change in Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity (CLASI-A) score from baseline to Week 24. Secondary efficacy endpoints include the proportion of participants who achieve 0 or 1 on the Cutaneous Lupus Activity Investigator's Global Assessment (CLA-IGA) scale at Week 24 (5-point Likert scale [0–4]), proportion of participants who achieve a $\geq$ 50% reduction in CLASI-A score from baseline at Week 24, and mean change in the Score of Activity and Damage in Discoid Lupus Erythematosus (SADDLE) from baseline to Week 24. Safety and tolerability of DAX will be assessed via the incidence of adverse events (AEs), serious AEs, and AEs of special interest. Pharmacokinetics and effects on pharmacodynamics and other biomarkers of interest will also be assessed.

Conclusion There is a significant unmet need for novel, fast-acting, and safe new therapies to reduce disease activity and damage and improve the quality of life for patients living with DLE. This is a proof-of-concept study that aims to evaluate a potentially new therapy in subjects with DLE.

403 TRENDS IN INCIDENCE AND PREVALENCE OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE AMONG PATIENTS WITH CUTANEOUS LUPUS ERYTHEMATOSUS FROM 2018–2020

[1]Henry W Chen*, [2]Jialiang Liu, [2]Donghan Yang, [2]Yang Xie, [3]Eric Peterson, [3]Ann Marie Navar*, [1]Benjamin F Chong*. *[1]University of Texas Southwestern Medical Center, Department of Dermatology, Dallas, TX, USA; [2]University of Texas Southwestern Medical Center, Quantitative and Biomedical Research Center, Department of Population and Data Sciences, Dallas, TX, USA; [3]University of Texas Southwestern Medical Center, Department of Internal Medicine, Division of Cardiology, Dallas, TX, USA; *Presenter; **Co-senior investigators*

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Background Autoimmune disease such as systemic lupus erythematosus (SLE) and psoriasis have been previously associated with an increased risk of atherosclerotic cardiovascular disease (ASCVD), though whether similar increased ASCVD risk is seen with cutaneous lupus (CLE) remains unclear. Thus, we sought to evaluate the prevalence and incidence of ASCVD among those with CLE, SLE, and psoriasis compared with disease-free controls.

Methods We performed a retrospective, longitudinal cohort study using outpatient and inpatient encounters claims data from the IBM® MarketScan® Commercial Claims database from January 2018 to December 2020. Our inclusion criteria included adults age $\geq$18 years with at least 1 year of continuous enrollment in the dataset. Within this population, we identified adults with CLE, SLE, and psoriasis based on the following International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes: CLE using L93, SLE using M32, and psoriasis using L40. CLE was further classified by subtypes: DLE (L93.0), SCLE (L93.1) and other CLE (L93.2). The control population included persons free of CLE, SLE, and psoriasis, matched 10:1 with the CLE population on age, sex, insurance type, and enrollment duration. Prevalent ASCVD was defined as coronary artery disease (CAD, I20 and I25), prior myocardial infarction (MI, I21 and I22), or cerebrovascular accident (CVA, I63 and select G43). Incident ASCVD (hospitalization