Background Treatment with ustekinumab (UST), an anti-IL-12/23, p40-neutralizing monoclonal antibody, improved global and organ-specific measures of disease activity in a randomized, placebo (PBO)-controlled trial of patients with active SLE (NCT02349061). Type I interferon (IFN-I) and type II IFN (IFN-gamma) are elevated in a subset of SLE patients. Although targeting IFN-I (anifrolumab) has demonstrated inconsistent efficacy and a preliminary study with anti-IFN-gamma mAb (AMG811) failed to establish benefit, we sought to determine if UST affects either pathway and if those effects correlated with a positive SRI-4 response at wk24.

Methods A phase-2, PBO-controlled study enrolled 102 adults with seropositive SLE (SLICC criteria) and active disease (baseline SLEDAI score 6 and 1 BILAG A and/or 2 BILAG B scores) despite standard-of-care therapy. Gene expression analysis using a 21 gene IFN-I gene signature (IGS) or IFN-gamma signature was performed by microarray analysis using whole blood Paxgene RNA samples. Serum IFN-gamma and IFN- levels were assessed using MSD (IFN-gamma) and Quantix (IFN-).

Results Serum IFN-gamma and IFN- and the IGS were elevated at baseline in SLE compared to healthy controls (p<0.0001). IGS was increased in approximately 67% of the SLE patients at baseline. No decrease was observed with IFN-protein or IGS levels after treatment with either UST or PBO. Whereas the proportion of patients achieving an SRI-4 response at wk24 was numerically greater in the IGS low patients (81.8% UST vs. 54.5% PBO) versus IGS high (48.6% UST vs. 20% PBO), the magnitude of the treatment effect (UST vs. PBO) was similar in both subsets (IGS low effect size=27.3% vs. IGS high effect size=28.6%). Despite similar baseline levels, UST-treated patients achieving an SRI-4 response at wk24 exhibited a significant decrease in IFN-gamma protein versus non-responders (p<0.05) at 4 and 8 wks and IFN-gamma gene signature at 4 wks (p<0.0001) and 24 wks (p<0.05) post-dosing.

Conclusions In this SLE trial population which had significant upregulation of IFN-I at baseline, clinical response to UST was not associated with IFN-I reduction. In contrast, a significant decrease in IFN-gamma protein and gene signature was associated with UST response. These findings suggest that a broad population of SLE patients may respond to UST regardless of baseline IFN-I status. Moreover, UST may have affected TH1 responses in SLE since IFN-gamma levels decreased following treatment.

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Non-SLE women are more likely to be up to date on pap screening compared to SLE women (48.59% vs 39.90% p=0.0117). SLE women who are up to date on pap screening and who have had previous positive HPV pap testing had a similar rate of HPV positivity compared to non-SLE patients (28.70% vs 20.60% p=0.163). There was a significant difference when we compared black SLE patients to white SLE patients with regards to overdue status (56.60% vs 43.49% p=0.0197), overdue status with prior HPV positivity in black SLE versus white SLE patients (70% vs 30% p=0.0455) and also higher rate of HPV positivity in black SLE versus white SLE patients (66.02% vs 33.97% p=0.0001). When we compared pap overdue black SLE vs black non-SLE we found higher number of black SLE patients were overdue versus black non-SLE (56% vs 46.36% p=0.0144) however the inverse was noted for white SLE and white non-SLE (43.39% vs 53.63% p=0.0263).

**Conclusions** This study suggests that women with SLE are at a significantly higher risk of falling behind on PAP smears when compared to women without SLE. Significant racial disparities between black SLE women and white SLE exist at our institution. Black SLE patients have a significant higher rate of HPV positivity compared to white SLE patients. Increased rate of HPV positivity and lower rates of screening in black SLE patients in conjunction with the known increased risk of cervical neoplasia due to SLE disease itself and due to immunomodulators used to treat SLE signifies that treating physicians should be mindful of the importance of preventative measures, such as cervical screening and HPV vaccination in the SLE population in particular black SLE patients.

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VALIDATION AND RELIABILITY OF A DISEASE-SPECIFIC QUALITY OF LIFE MEASURE IN PATIENTS WITH CUTANEOUS LUPUS ERYTHEMATOSUS

Motolani E. Ogunsanya,1 Stephanie K. Cho,2 Andrew Hudson,3 Benjamin F. Chong*. 
1 College of Pharmacy, University of Oklahoma Health Sciences Center; 2 Department of Dermatology, University of Texas Southwestern Medical Center; 3 Texas Tech University Health Sciences Center

Background Cutaneous lupus erythematosus (CLE) is a potentially disfiguring, chronic autoimmune disease with variable skin manifestations, negatively affecting the quality of life (QoL) of patients. Patient-reported outcome (PRO) measures used in assessing QoL in CLE patients have been either generic or developed without input from patients with CLE. The objective of this study was to demonstrate the reliability and validity of a disease-specific QoL measure for CLE (CLEQoL).

Methods A total of 101 patients with a diagnosis of CLE were recruited at outpatient dermatology clinics at the University of Texas Southwestern Medical Center and Parkland Health and Hospital System in Dallas, TX. Each patient was asked to complete the CLEQoL and Short Form 36 (SF-36). The CLEQoL contains 29 questions from the SKINDEX, a generic skin disease QoL measure, three questions relating to photosensitivity and alopecia (adapted from the SKINDEX-29+3), and four questions from the vitiligo-specific quality of life (VitiQoL) (figure 1). These questions were validated via focus groups of patients with CLE. Internal consistency was used as a measure of reliability. Validity was measured in two ways structural validity via exploratory factor analysis and convergent validity via Spearman correlations between CLE-QoL and SF-36. Patient demographic and disease characteristics were collected. Data was analyzed using SPSS and significance was set to $p<0.05$.

Results The average age of our CLE patients was 48±13 with discoid lupus (n=72, 71.3%) being the most predominant CLE subtype. Patients were mostly female (n=88, 87.1%) and African-American/Black (n=59, 58.4%). Internal consistency ranged from 0.67 to 0.95. A total of five domains, functioning, emotions, symptoms, body image/cosmetic effects and photosensitivity, were extracted with a total explained variance of 71.06%. CLEQoL-related domains correlated with SF-36 domains (r ranging from $0.39$ to $0.65$). The Cutaneous Lupus Activity and Severity Index (CLASI) activity scores correlated positively with the CLEQoL functioning (r=0.24, p<0.05), emotions (r=0.26, p<0.05), and symptoms (r=0.32, p<0.05) domains. CLASI damage scores correlated positively with the CLEQoL body image/cosmetic effects (r=0.41, p<0.001) and photosensitivity (r=0.25, p<0.05).

Conclusions The CLEQoL was found to be a valid and reliable PRO measure for assessing QoL in patients with CLE. Demonstrating that the CLEQoL has strong psychometric properties is an important step towards the development of a disease-specific PRO measure for future CLE clinical trials.

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