literature review to identify items that reflect the construct of damage in SLE and grouped the items into organ domains. Each domain was reviewed by paediatric rheumatologists.

Snow-ball sampling was used among SLICC members, asking them to nominate 3–4 SLE experts considering a range of clinical expertise, equality, diversity and inclusiveness factors, and the global nature of SLE research. The LFA, Lupus UK, Lupus Europe and Lupus Canada were also asked to nominate 4-6 patient/carer representatives to participate in the Delphi exercise. Participants were asked to nominate items that should be included in a revised damage index based on the updated construct definition1 using a free-text option in the Delphi exercise.

Results We established a group of 146 individuals (mean age 50.6 ranging from 28 to 79 years; 60.3% females; 58.9% white; clinical experience from 1 to 51 years) from 35 countries, broadly representative of the lupus research and patient community. There were 135 medical doctors, 2 allied health professionals and 9 patients. Of 135 medical doctors, 120 were rheumatologists, 7 internists, 5 nephrologists, 2 dermatologists, and 1 immunologist. The response rate after the first round Delphi exercise was 97.9%.

All items in the original SDI were nominated in both processes. Item generation yielded approximately 2,600 items. After rationalising for repetition, redundancy, and harmonisation of synonyms, 220 unique items were identified across 14 organ systems. The literature review proposed 4 (1.8%) unique items, 103 (46.8%) unique items were from the Delphi only and 113 (51.4%) items appeared in both exercises (figure 1).

Conclusion Using a combined data-driven and expert/patient-based approach, items and domains that comprise damage in SLE have been expanded. Just over half of all items were nominated by both approaches. However, the Delphi exercise which included a wide and diverse group of contributors, provided a large number of unique items for further consideration. Our data confirms the value of large group exercises early in such a process to maximise the scope of new items to consider for a revised index.

REFERENCE

Lay Summary The SLICC/ACR Damage Index (SDI) (published in 1996) is widely used in clinical studies and trials to measure the long-term complications that can occur in lupus patients, such as cataracts, fractures, and kidney failure. Higher scores are associated with poorer quality of life, as reported by patients. A number of drawbacks have also been found with the SDI. We need to better understand and measure the impact of these complications from a patient and doctor’s perspective to get a much deeper understanding of how SLE affects people. We used two methods to generate new items to include in an updated SDI. First, we used the medical literature to identify possible complications of lupus. Then, we asked a large group of lupus experts and patients to nominate complications. The process generated approximately 2,600 items. After removing redundant suggestions, 220 unique items were identified. The literature review proposed 4 (1.8%) unique items, 103 (46.8%) unique items were from the large group only and 113 new (51.4%) items appeared in both exercises. Our data shows the value of large group exercises that include patient representatives, to maximise the scope of new items to consider for a revised index.
p values < 0.05, ranking genes by log2FoldChange, and running WebGestalt. For clinical outcomes, outliers were identified and dropped per cell type and differential expression analysis was run using raw counts from Telescope with DESeq2 per cell type, adjusting for race, lane, sex, and immunosuppressant use at the time of blood draw.

Outcomes studied included disease activity (SLEDAI score), autoantibody production (dsDNA, RNP, Sm), ACR renal criteria and disease severity as defined by clinical clusters previously described in the same SLE participants, (Lanata et al, Nat Commun, Aug 29 2019;10(1):3902).

**Results**

A total of 26,768 HERVs/LINEs were detected across the 480 samples. These were mostly cell-specific (figure 1). High HERVs/LINEs expression correlated with host gene transcription in a cell specific manner. Significant associations with retroviral load include differentially expressed genes in pathways of: olfactory signaling pathway, regulation of IFNA signaling, and interferon alpha/beta signaling in CD14 cells; DNA repair and host response of HIV factors in CD4 cells; activation of HOX genes and antimicrobial peptides in CD19 cells; and regulation of complement cascade, neutrophil degranulation and several metabolic pathways in NK cells (figure 2). Significant associations between HERVs/LINEs expression and clinical outcomes are summarized in table 1. We found that CD19 cells had the most robust associations with disease severity, SLEDAI score, history of renal disease, and autoantibody production (FDR p<0.05). Other findings included high

<table>
<thead>
<tr>
<th>HERVs/LINEs counts</th>
<th>CD4</th>
<th>CD14</th>
<th>CD19</th>
<th>NK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti Sm antibody production</td>
<td>Up</td>
<td>Down</td>
<td>Up</td>
<td>Down</td>
</tr>
<tr>
<td>Disease severity (severe 2 cluster vs mild cluster)</td>
<td>2</td>
<td>15</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>History of renal disease</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Anti-RNP antibody production</td>
<td>6</td>
<td>7</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Anti-dsDNA antibody production</td>
<td>35</td>
<td>2</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Disease activity (SLEDAI score)</td>
<td>1</td>
<td>15</td>
<td>2</td>
<td>13</td>
</tr>
</tbody>
</table>

**Abstract 606 Table 1** HERVs/LINEs expression associated with clinical outcomes, adjusted for sex, race and immunosuppressive medication use in 120 SLE participants. (FDR p<0.05)

**Congress, date, location**

Lupus 21st Century, September 20, 2022 – September 23, 2022, Loews Ventana Canyon Resort

**Congress website**

https://web.cvent.com/event/a6cd0d72-4b4e-40a4-939b-c133c05df3af/

**Abstract guidelines**

https://web.cvent.com/event/a6cd0d72-4b4e-40a4-939b-c133c05df3af/websitePage:795426fe-0fc9-44d7-9156-b30723c39052

**Submission category**

- Genetics
- Nucleic Acids in SLE
- The Macrophage in SLE
- Lupus Nephritis
- Brain Injury in SLE
- Pharmacoepidemiology
- Clinical Research in SLE
- Covid-19
- Cutaneous SLE
- SLE Diagnosis
- Lupus-Targeted Therapeutics
- Cardiovascular Disease and Lupus
- PROs
- Biomarkers in Clinical Trials
- B Cells
- Transcriptomics
- T Cells
- Innate Immunity
- Autoantibodies
- Microbiome

**Presentation preference**

N/A

**Character/word limit**

No limit stated, will ask congress to confirm

**Figures/tables Allowed**

- No limit stated, will ask congress
- Embed in abstract word doc

**Swastika**

N/A

**Style**

- A lay summary is required – see separate Lay summary file
- Not needed at submission

**Submission deadline**

August 1, 2022 at 11:59 PM ET
HERVs/LINEs expression in NK cells in patient with severe disease, and in CD4 cells in patients with dsDNA production (FDR p<0.05).

Conclusion HERVs/LINEs expression is associated with gene expression in a cell specific manner. Further, we demonstrated a strong association between HERVs/LINEs expression and clinical outcomes, particularly in CD19 cells, in SLE patients.

Clinical Research in SLE

IMPACT OF ANIFROLUMAB ON NEUROPSYCHIATRIC MANIFESTATIONS OF DEPRESSION AND SUICIDALITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Susan Manzi, Catharina Lindholm, Hor Hupka, Lijin (Jinny) Zhang, Manish Shroff, Gabriel Abreu, Shanti Werther, Raj Tummala. 1Lupus Center of Excellence, Autoimmunity Institute, Allegheny Health Network, Rheumatology, Pittsburgh, PA, USA; 2Clinical Development, Late Respiratory and Immunology, BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden; 3Clinical Development, Late Respiratory and Immunology, BioPharmaceuticals R&D, AstraZeneca, Warsaw, Poland; 4Global Patient Safety, BioPharmaceuticals R&D, AstraZeneca, Gaithersburg, MD, USA; 5Global Patient Safety, Vaccines and Immune Therapy, RandD, AstraZeneca, Boston, MA, USA; 6Biometrics, Late Respiratory and Immunology, BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden; 7Global Patient Safety, BioPharmaceuticals R&D, AstraZeneca, Gaithersburg, MD, USA; 8Clinical Development, Late Respiratory and Immunology, BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden.

Background Neuropsychiatric (NP) disease is more common in patients with systemic lupus erythematosus (SLE) than in the general population. Increased incidence of NP events (depression and suicidality) has been reported with biologic therapies, including SLE therapies. Depression and suicidality were evaluated in patients with SLE treated with anifrolumab, a type 1 interferon receptor antibody, in the TULIP-1 and TULIP-2 trials. This analysis aims to understand the impact of anifrolumab treatment on NP manifestations (depression and suicidality) in patients with SLE relative to standard therapy using pooled data from the TULIP trials.

Methods TULIP-1/-2 were randomized, placebo-controlled, 52-week trials of intravenous anifrolumab every 4 weeks in patients with moderate to severe SLE despite standard therapy. Patients with active severe or unstable NP SLE were excluded. Patients who received ≥1 dose of anifrolumab 300 mg or placebo were analyzed for depression and suicidality.

Results In the TULIP pooled analysis, 360 patients received anifrolumab and 365 received placebo. Mean PHQ-8 scores were in the mild range (5 to <10); 9.7 in both groups at baseline (table 1). Excluding patients taking antidepressants, mean PHQ-8 scores were 9.5 in the anifrolumab group and 9.7 in the placebo group at baseline. No clinically meaningful worsening in mean PHQ-8 scores was observed from baseline to Week 52 in the anifrolumab (–2.0) or placebo (–1.3) groups; excluding patients taking antidepressants, mean changes in PHQ-8 were –2.0 and –1.2, respectively. Depression AEs during the study were reported in 11 anifrolumab- and 9 placebo-treated patients. At baseline, antidepressant use was comparable between groups (anifrolumab group, 7 patients [1.9%]; placebo group, 6 patients [1.6%]).