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 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.

Abstract 605 Figure 1 Number of candidate items for the revised organ damage index from literature review and the first round Delphi exercise.

REFERENCE

1. Johnson, S. R *et al*. Evaluating the construct of damage in SLE. *Arthritis Care Res*. 2021.

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.

606 CELL-SPECIFIC HUMAN ENDOGENOUS RETROVIRUS EXPRESSION, HOST GENE EXPRESSION AND SLE PHENOTYPES

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10.1136/lupus-2022-lupus21century.27

Background/purpose Human endogenous retroviruses (HERVs) and long interspersed nuclear elements (LINEs) make up 5-8% and 21% of the human genome. Their expression may contribute to production of type I interferon and the generation of autoantibodies. The objective of this study was to detect

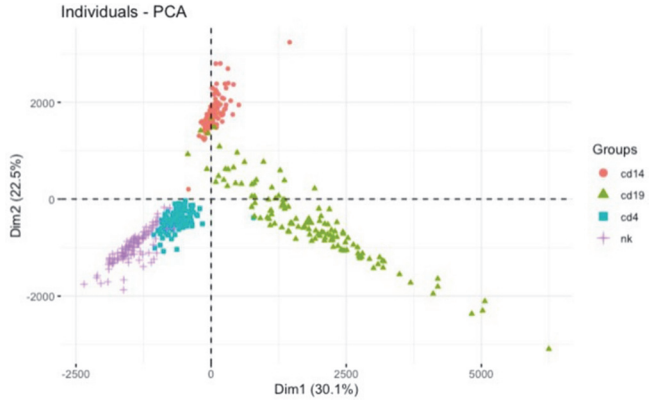
HERVs and LINEs in 4 cell-types in SLE patients and characterize their relationship to host gene expression and SLE phenotypes.

Methods Peripheral blood mononuclear cells were isolated from 120 deeply-phenotyped SLE participants. Cells were sorted utilizing magnetic beads (CD14+ monocytes, B cells, CD4+ T cells, and NK cells) and STEM cell technologies for a total of 480 samples. Libraries were sequenced on a HiSeq4000 PE150. Trimmed fastq files were aligned to GRCh38 release 104 using default settings with STAR to generate alignment files. Alignment files were converted to gene counts using featureCounts. Raw counts from *Telescope* were normalized using DESeq2 and summed per patient; patients were then separated into tertiles based on the summed counts for HERVs and LINEs. DESeq2 was used to perform differential gene expression analysis using gene counts from featureCounts, comparing the third to the first tertile. Gene set enrichment analysis was performed using genes with adjusted

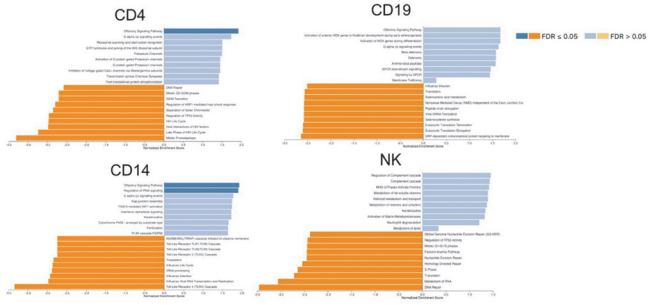
p values < 0.05, ranking genes by log2FoldChange, and running WebGestalt. For clinical outcomes, outliers were identified and dropped per cell type and differential expression analysis was run using raw counts from *Telescope* with DESeq2 per cell type, adjusting for race, lane, sex, and immunosuppressant 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



Abstract 606 Figure 1 PCA plot of HERVs and LINEs expression in 4 cell types of 120 SLE individuals.



Abstract 606 Figure 2 Pathways of differentially expressed genes associated with high HERVs/LINEs expression per cell type in 120 SLE patients.

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)

	HERVs/LINEs counts							
	CD4		CD14		CD19		NK	
	Up	Down	Up	Down	Up	Down	Up	Down
Anti Sm antibody production	5	8	5	7	21	27	2	7
Disease severity (severe 2 cluster vs mild cluster)	2	15	4	10	1087	44	461	0
History of renal disease	1	4	2	1	5	12	0	0
Anti-RNP antibody production	6	7	4	8	17	9	1	0
Anti-dsDNA antibody production	35	2	5	2	21	11	0	0
Disease activity (SLEDAI score)	1	15	2	13	2	227	0	1

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/summary
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
References Style	N/A
Other points	A lay summary is required – see separate Lay summary file
Disclosures	Not needed at submission
Other	
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

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

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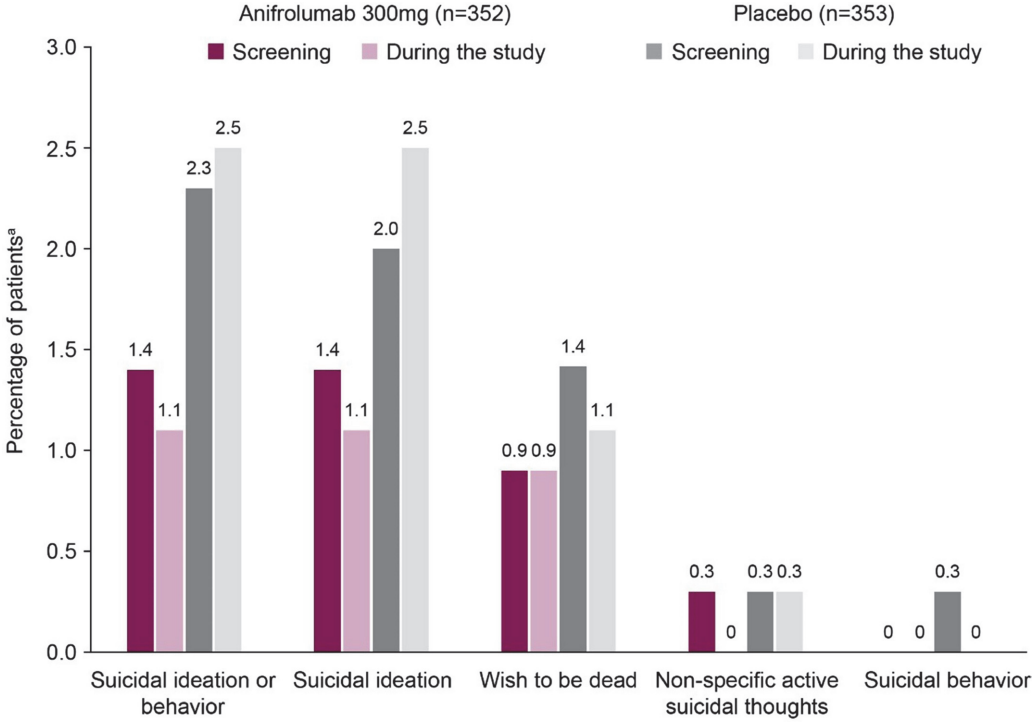
Background Neuropsychiatric (NP) disease is more common in patients with systemic lupus erythematosus (SLE) than in the general population.[1] Increased incidence of NP events (depression and suicidality) has been reported with biologic therapies, including SLE therapies.[2] Depression and suicidality were evaluated in patients with SLE treated with anifrolumab, a type I interferon receptor antibody, in the TULIP-1 and TULIP-2 trials.[3,4] 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.[3,4]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 .[3,4] The Personal Health Questionnaire Depression Scale-8 (PHQ-8) and Columbia Suicide Severity Rating Scale (C-SSRS) were used to assess clinical depression and suicidal ideation and behavior, respectively. Incidence of adverse events (AEs) within the standardized Medical Dictionary for Regulatory Activities query of depression (excluding suicide and self-injury) and antidepressant use at baseline and during the study were also assessed.

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-treated patients (3.1%) and 9 patients who received placebo (2.5%). At baseline, antidepressant use was comparable between groups (anifrolumab group, 7 patients [1.9%];



Abstract 607 Figure 1 C-SSRS summary, excluding patients taking antidepressants. [a]Percentages are based upon all patients included in the analysis within the respective pool and treatment group.