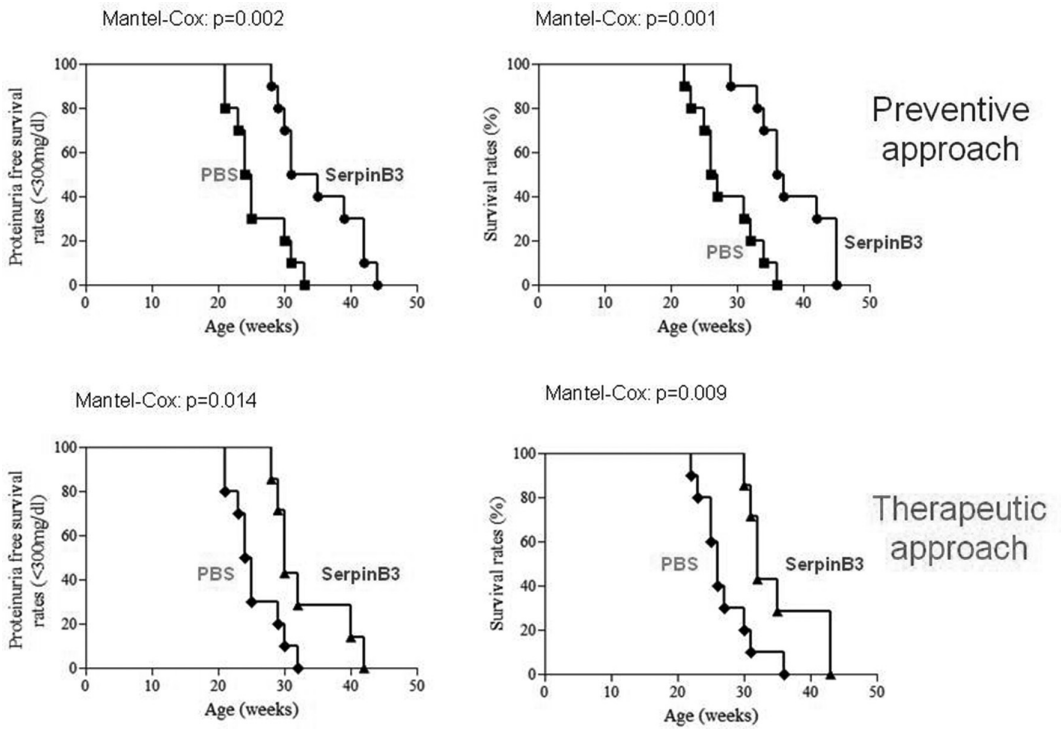

Abstract S7A:7 Figure 1 Survival in NZB/W F1 brought to natural death

Methods NZB/W F1 and MRL/lpr mice were used. 40 NZB/W F1 mice were divided into 4 groups of 10 mice each and intraperitoneally injected twice a week starting before occurrence of proteinuria traces (group 1 and 2, prophylactic approach) or after development of proteinuria 30 mg/dl (group 3 and 4, therapeutic approach) with hrSERPINB3 (7.5 µg/0.1 mL prophylactic approach, or 15 µg/0.1 mL therapeutic approach) or PBS (0.1 mL). 20 MRL/lpr mice were injected with hrSERPINB3 (group 5, n=10) or PBS (group 6, n=10) with a prophylactic approach. We assessed time of occurrence and titers of anti-dsDNA and anti-C1q antibodies by ELISA; proteinuria and serum creatinine; overall- and proteinuria-free survival. Six NZB/W F1 mice were sacrificed at week 27, while 10 MRL/lpr mice at week 13 and another 10 at 16/18 weeks for histological kidneys comparison. Flow-cytometry was performed on MRL/lpr splenocytes.

Non parametric tests were performed for statistics; proteinuria-free (<300 mg/dl) and overall survival were evaluated by Kaplan-Meier method.

Results Levels of autoantibodies were significantly decreased and delayed in group 1 vs group 2, group 3 vs group 4, and group 5 vs group 6 ($p<0.0001$ for all). Proteinuria levels were significantly reduced and proteinuria-free and overall survival were significantly improved in SERPINB3 groups vs controls (figure 1). No differences were found among creatinine serum levels. Histological analysis showed a lower prevalence of severe tubular lesions in group 5 vs group 6 MRL/lpr mice at week 16 (chi-squared $p=0.014$), and mice belonging to SERPINB3 groups showed a trend toward a reduced prevalence of severe glomerular and tubular lesions. Th17:Treg ratio significantly decreased due to a remarkable increase in Treg levels in MRL/lpr mice treated with SERPINB3.

Conclusions Administration of SERPINB3 significantly improves disease and delays the onset of severe glomerulonephritis in lupus-prone mice. SERPINB3 may influence immune-cell function through immunoregulatory effects involving promotion of Treg.

S7A:8 EFFICACY AND SAFETY OF USTEKINUMAB, AN INTERLEUKIN 12/23 INHIBITOR, IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS OF A PHASE 2, RANDOMISED PLACEBO-CONTROLLED STUDY

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Purpose IL12 and IL23 pathway have been linked to SLE pathogenesis. Anti-IL12/23 monoclonal antibody ustekinumab (UST) previously approved for psoriasis, psoriatic arthritis, and Crohn's diseasewas evaluated in pts with active SLE.

Methods A Ph2, PBO-controlled study in 102 adults with seropositive SLE by SLICC criteria with active disease despite standard-of-care therapy were randomised to UST vs PBO, added to standard care. Primary endpoint was the proportion achieving SLE response index (SRI)−4 response at wk24. Secondary endpoints included change SLEDAI-2K, Physician's Global Assessment (PGA), and BICLA response.

Results The mITT population (includes pts who received at least one dose) at wk24 revealed 60% of UST pts with SRI-4 response vs 31% in PBO ($p=0.0046$). Pts in UST group had greater median change from wk0 to wk24 in SLEDAI-2K and PGA vs PBO (table 1). No difference was observed in BICLA composite response at wk24, but more UST pts had no BILAG worsening vs PBO. Through wk24, 78% of UST pts and 67% of PBO pts had greater than or equal to 1 AE; 8.3%–9.5%, respectively, had greater than or equal to 1 SAE (table 1). There were no deaths in the study. Safety events

were consistent with UST safety profile in other studied indications.

Conclusion UST showed efficacy in treatment of active SLE vs PBO and comparable safety warranting further investigation. UST may work via a novel mechanism of action in SLE.

Abstract S7A:8 Table 1 Efficacy and safety results at week 24

	Placebo	Ustekinumab
Patients randomized, n	42	60
Efficacy		
Patients with SRI-4 response, n (%)	13 (31.0)	36 (60.0)
P value		0.0046*
Change from baseline in SLEDAI-2K, median (range)	-2.0 (-20; 10)	-6.0 (-10; 3)
P value		0.0265*,§
Change from baseline in PGA, median (range)	-1.6 (-5.6; 2.7)	-2.5 (-6.6; 2.8)
P value		0.2116*,§
Patients with BICLA response, n (%)	14 (33.3)	21 (35.0)
P value		0.9939*
Proportion of BICLA nonresponders with no BILAG worsening, n/N (%)	11/28 (39.2)	29/39 (74.4)
P value		0.0043
Patients with 50% improvement from baseline joint disease activity‡, % (95% CI)	63.2 (61.7-64.6)	87.7 (86.8-88.6)
P value		0.0208§
Patients with 50% improvement from baseline CLASI activity score‖, % (95% CI)	25.2 (23.1-27.4)	58.7 (57.4-60.1)
P value		0.0429*
Change from baseline in anti-dsDNA (kIU/L)¶, median (range)	-12.6 (-168.8; 233.1)	-30.7 (-2919.6; 132.9)
P value		0.1075§
Change from baseline in Complement C3 (mg/dL)#, median (range)	0.15 (-12.4; 21.8)	6.60 (-17; 50.8)
P value		0.0636§
Adverse events		
Patients with ≥1 TEAE, n (%)	28 (66.7)	47 (78.3)
Most Common TEAEs, n (%)		
Upper respiratory tract infection	9 (21.4)	5 (8.3)
Urinary tract infection	5 (11.9)	6 (10.0)
Nasopharyngitis	3 (7.1)	6 (10.0)
Headache	5 (11.9)	4 (6.7)
Patients with ≥1 SAE, n (%)	4 (9.5)	5 (8.3)

*Prespecified analyses; all other analyses shown here were post-hoc.
§One-sided test for no difference between two treatment groups based upon a Wilcoxon non-parametric median test for difference of location
‡Patient subpopulation (67% of total population) with at least 4 joints with pain and signs of inflammation at baseline
‖Patient subpopulation (58% of total population) with CLASI activity score of at least 4 at baseline
¶Proportions of responders and p values based on a modified intention-to-treat analysis using a multiple imputation model for missing data from weeks 16 to 24
Patient subpopulation (42% of total population) with anti-dsDNA autoantibodies present at baseline
#Patient subpopulation (41% of total population) with low Complement C3 levels present at baseline
One-sided test for no difference between two treatment groups based upon a Wilcoxon non-parametric median test for difference of location
BICLA, BILAG-based Combined Lupus Assessment; BILAG, British Isles Lupus Assessment Group; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; ; PGA, physician's global assessment; SRI-4, SLE Response Index; TEAE, treatment emergent adverse event

S7d – PRO

S7D:4 THE RELATIONSHIP BETWEEN HEALTH-RELATED QUALITY OF LIFE AND REMISSION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A LONGITUDINAL COHORT STUDY

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Aim To investigate the relationship between health-related quality of life (HRQoL) and remission as a target in a treat-to-target approach of systemic lupus erythematosus (SLE) in a longitudinal observational cohort study.

Methods HRQoL was assessed with the physical and mental component score (PCS and MCS, respectively) of the SF-36 questionnaire and adjusted for the Dutch general population (mean 50±10). DORIS remission categories (no remission/remission on therapy/remission off therapy) were applied 1. Determinants of PCS and MCS were identified with simple linear regression analyses. Association between remission and HRQoL was assessed with General Equation Estimation (GEE) models.

Results Data from 154 patients with 2 years of follow-up were analysed. Patients were mostly female (89%) and Caucasian (69.5%). Remission off therapy was present in 27.3% of patients, 18.1% were in remission on therapy, and 54.5% were not in remission. Mean PCS at baseline was 38.1 (±11.1) and mean MCS was 46.3 (±10.6). Patients in remission (as defined by remission on or off therapy) had higher SF-36 scores in all subdomains compared to patients not in remission. PCS was positively associated with employment and remission, while negatively associated with ESR, patient global assessment, SLE-damage- index, prednisone use, immunosuppressant use, and body mass index. MCS was positively associated with Caucasian ethnicity and negatively associated with patient global assessment.

PCS at the last visit was higher in patients in remission during 2 years (n=44) compared to patients (n=44) who were never in remission during 2 years of observation (mean 45.9 vs mean 36.8, p<0.001, respectively).

In GEE analysis, a gradual and statistically significant increase of PCS was observed from patients not in remission (mean PCS 36.0) to remission on therapy (41.8) to remission off therapy (44.8). No significant difference in MCS was found between remission states.

Conclusion We show a longitudinal relationship between PCS – but not MCS – and remission, which supports the validity of DORIS remission criteria as a treatment goal in SLE. A lack of association between MCS and remission might be explained by near-normal MCS scores in our cohort. Secondly, non-disease related factors might more importantly influence MCS.

S7D:5 THE DIAGNOSTIC PHASE OF LUPUS – BEING IN A STANDSTILL-OF-LIFE

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Purpose To investigate the changes in basic life conditions over time from the perspective of female patients with systemic lupus erythematosus (Lupus). This presentation concerns experiences around the diagnostic phase of Lupus.

Method From 2013 to 2015, 43 individual interviews were performed with 15 female patients. Data were analysed according to the methodology of Human Science Phenomenology, which aims at collecting a common meaning-structure of human experiences. By considering basic condition of time, space, body and relationships, deeper knowledge of patient experiences can be reached.

Results Mean age was 45.6 years and mean disease duration 14.8 years. The time to diagnosis after the first symptoms varied from 2–54 months (mean: 21 months, SD: 16 months). The essential experience of going through the diagnostic phase was found to be in a Standstill-in-life constituted by three existential themes:

1. The experience of an altered perception of time and space while being exposed to the many medical examinations and tentative diagnosis situated the patient in a passive stance while waiting for clarification.
2. The acute or changing symptoms made daily life uncertain as the normal bodily reliance changed and interpreted as standing on an uneven ground.
3. Having the final Lupus diagnosis represented a deep existential change in personal relationships with self and others, and marked a substantial turning point in life.

Conclusion The diagnostic phase of Lupus is often protracted over several years. This study shows how going through the diagnostic phase initiates a significant change in the basic life