Background/purpose Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K) is one of the most commonly used disease activity indices in clinical practice and research but this index doesn't account for severity within each descriptor. Moreover, in clinical trials, the use of standard of care (SoC), which includes glucocorticosteroid (GCS) often confounds trial results.

We developed and validated a novel lupus disease activity index, SLEDAI-2K GCS (SLEDAI-2KG), that describes disease activity while accounting for GCS dose. SLEDAI-2KG has the same descriptors as SLEDAI-2K in addition to a new descriptor 'GCS' with different weight scores based on the dose of GCS. Furthermore, SLEDAI-2KG has a low administration burden and a simple scoring system similar to SLEDAI-2K. We aimed to compare the performance of SLEDAI-2K and SGI in identifying responders in response to SoC.

Methods Patients have been followed prospectively according to a standard protocol between January 2011 and January 2014, at a single lupus centre, with active disease (SLEDAI-2K $\geq$ 6), on prednisone $\geq$ 10 mg/day, and with follow up visits within 5–24 months were studied. Treatment was determined based on the judgment of the treating rheumatologist.

Response to SoC therapy, at first follow up visit, was assessed by SLEDAI-2K and SLEDAI-2KG. Responders were defined based on the decrease in SLEDAI-2K and SGI score by $\geq$ 4. The performance of SLEDAI-2K and SGI was also compared using different cut-off points; 5, 6 and 7. Descriptive analysis was used.

Results 111 patients met the inclusion criteria of the study and were further analysed. Patients' characteristics are represented in table 1.

SLEDAI-2KG identified more responders at 6 months (94% vs 84%) and at 12 months (92% vs 76%) compared to SLEDAI-2K by cut off of 4. SLEDAI-2KG also identified more responders with cut off points 5, 6 and 7 (table 2).

Abstract S1D:5 Table 1 Patients characteristics

Variables	Total (n=111)
Sex (female)	98 (88.3%)
Age at baseline (mean $\pm$ SD)	35.75 $\pm$ 11.51
SLE duration at baseline (mean $\pm$ SD)	9.02 $\pm$ 7.74
Ethnicity	
Asian	13 (11.7%)
Black	23 (20.7%)
Caucasian	51 (45.9%)
Others	24 (21.6%)
Months from baseline to 1 st follow-up (mean $\pm$ SD)	7.68 $\pm$ 2.95
SLEDAI-2K at baseline (mean $\pm$ SD)	12.39 $\pm$ 6.03
Prednisone dose at baseline (mg/day) (mean $\pm$ SD)	22.94 $\pm$ 14.19
SLEDAI-2KG at baseline (mean $\pm$ SD)	17.48 $\pm$ 6.78
SLEDAI-2K at 1 st follow-up	8.08 $\pm$ 6.04
Prednisone dose at 1 st follow-up (mg/day) (mean $\pm$ SD)	15.23 $\pm$ 10.94
SLEDAI-2KG at 1 st follow-up	12.67 $\pm$ 6.98

Conclusion The novel index, SLEDAI-2KG, is superior to SLEDAI-2K in identifying responders at 6 and 12 months accounting for steroid dose and thus adjusting for severity within each descriptor of SLEDAI-2K. SLEDAI-2KG has the ability to enhance analyses in clinical trials to differentiate between responders on minimal and moderate/large doses of GCS.

Abstract S1D:5 Table 2 Responders by SLEDAI-2K and SLEDAI-2KG in 111 patients

Indices	Percentage of responders at 6 months					Percentage of responders at 12 months				
	$\geq$ 3	$\geq$ 4	$\geq$ 5	$\geq$ 6	$\geq$ 7	3	4	5	6	7
SLEDAI-2K	84%	84%	68%	68%	59%	77%	76%	57%	55%	44%
SLEDAI-2KG	95%	94%	88%	83%	79%	93%	92%	80%	70%	62%
Additional Responders	11%	10%	20%	15%	20%	16%	16%	23%	15%	18%

S1D:6 TARGETING PLASMA CELLS AND THEIR PRECURSORS BY IMMUNOABLATION VERSUS BORTEZOMIB PLUS RITUXIMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Purpose To investigate the therapeutic relevance of targeting long-lived plasma cells (PC), which contribute to the chronicity of SLE through continuous secretion of pathogenic antibodies, using immunoablation with antithymocyte-globulin (ATG) in the context of haematopoietic stem cell transplantation (HSCT) or proteasome inhibition with Bortezomib.

Methods Prospective analysis of outcome in 10 SLE patients after receiving autologous HSCT between 1998 and 2012 and 8 SLE patients after receiving a median 2 cycles (range 1–4) of Bortezomib 1.3 mg/m² between 2009 and 2012 at the Charité – University Medicine Berlin. Multiparametric flow cytometry was applied to characterise peripheral blood or bone marrow PC subsets and B cells. Autoantibodies and vaccine titres were investigated with ELISA.

Results In all HSCT treated patients clinical remissions (SLEDAI <3) were achieved, accompanied by a complete normalisation of anti-dsDNA antibody titres (92.6% reduction) and a significant reduction of antinuclear antibodies and vaccine titres (measles 82.3%). Peripheral blood B and PCs were virtually absent and bone marrow PCs largely depleted (97.6% reduction, n=1) shortly after HSCT and regenerating B cells almost exclusively displayed a naïve phenotype. Upon proteasome inhibition, clinical improvements were associated with a significant reduction of anti-dsDNA autoantibodies (69.3%) and vaccine titers (measles 32.5%). While B cell number/phenotype remained stable, both bone marrow and circulating PC were significantly reduced (~50%) but rapidly regenerated after proteasome inhibition, which could be prevented by additional rituximab therapy in one patient applied.

Conclusions Although less prominent compared to HSCT, proteasome inhibition with Bortezomib promoted a therapeutically relevant PC depletion in refractory SLE. Nevertheless, for sustained responses, PC depletion needs to be combined with therapeutic strategies targeting their precursor B cells, e.g. with rituximab, as indicated by our preclinical studies in murine lupus.

S2a – Prediction & prevention

S2A:4 VALIDATION OF REMISSION AND LUPUS LOW DISEASE ACTIVITY STATE AS PREDICTORS OF ORGAN DAMAGE IN SLE

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Background/purpose Outcome measures that combine control of SLE activity and prednisone reduction are clinically relevant. A clinical goal in SLE is to reduce risk of long-term organ damage. We assessed whether two recently proposed disease activity outcomes were predictive of future damage.

Methods For each month of follow-up in a large SLE cohort, we determined whether the patient was in Clinical Remission (as defined by the DORIS working group) or lupus low disease activity state (LLDAS) (as defined by Franklyn *et al.*). Clinical Remission was defined as a PGA<0.5, clinical SLEDAI=0 and no prednisone or immunosuppressants. Clinical Remission on Treatment allowed for prednisone ≤5 mg/day and immunosuppressant use. LLDAS was defined as a SLEDAI ≤4, PGA≤1.0, no major organ activity, and no new activity. LLDAS on treatment allowed for prednisone use ≤7.5 mg/d and immunosuppressants. Damage was defined using the SLICC/ACR Damage index.

Results There were 81 118 person-months observed among 2026 patients (92% female, 53% Caucasian, 39% African-American). Table 1 shows the rates of damage, per person month, in subgroups defined by Remission or LLDAS.

Damage rates were relatively low when LLDAS was achieved at least 50% of the time. These rates were similar to those experienced by patients who met a more stringent treatment restriction with Remission on Treatment at least 50% of the time.

Conclusion Percent time in LLDAS had a clear dose response for rate ratios of organ damage. The equivalence of LLDAS and DORIS remission on treatment is welcome news, as LLDAS on treatment >50% of the time is an easier goal to achieve (3 times more person-months observed in our cohort) and more realistic as a clinical trial outcome.

Abstract S2A:4 Table 1 Rates of new damage, in subgroups defined by past levels of disease activity

Percentage of Prior Months in:	Number of person-months observed	Number of months with an increase in SLICC/ACR Damage Index	Rate of damage per 100 person months	Rate Ratios	P-values
Clinical Remission	-	-	-	-	-
None	35,772	406	1.13	1.0 (Ref)	-
Not none, but < 25%	14,358	102	0.71	0.60 (0.48,0.75)	<0.0001
25% to 50%	6573	50	0.76	0.66 (0.46,0.94)	0.023
50% to 75%	3845	27	0.70	0.63 (0.42,0.97)	0.035
75%+	1,641	10	0.61	0.58 (0.30,1.15)	0.12
Clinical Remission on Treatment	-	-	-	-	-
None	16,491	250	1.52	1.0 (Ref)	-
Not none, but < 25%	20,169	170	0.84	0.54 (0.44,0.67)	<0.0001
25% to 50%	14,344	103	0.72	0.46 (0.36,0.60)	<0.0001
50% to 75%	8396	54	0.64	0.43 (0.30,0.60)	<0.0001
75%+	2,789	18	0.65	0.45 (0.27,0.75)	0.0019
LLDAS	-	-	-	-	-
None	30,366	343	1.13	1.0 (Ref)	-
Not none, but < 25%	10,880	106	0.97	0.86 (0.69,1.07)	0.18
25% to 50%	5012	40	0.80	0.70 (0.51,0.98)	0.037
50% to 75%	8494	60	0.71	0.63 (0.48,0.83)	0.0010
75%+	7,527	46	0.61	0.54 (0.40,0.73)	<0.0001
LLDAS on Treatment	-	-	-	-	-
None	7,656	117	1.53	1.0 (Ref)	-
Not none, but < 25%	10,555	134	1.27	0.83 (0.65,1.06)	0.14
25% to 50%	12,686	129	1.02	0.66 (0.51,0.85)	0.0013
50% to 75%	18,151	133	0.73	0.48 (0.37,0.61)	0.0010
75%+	13,141	82	0.62	0.40 (0.30,0.54)	<0.0001