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