severe forms of lupus continues to this day. One of the treatment highlights of the modern era came in the late part of the twentieth century with the approval of mycophenolate mofetil for acute kidney transplant rejection. Shortly thereafter in the early part of the twenty-first century, it was adopted as standard of care to rival cyclophosphamide for lupus nephritis, although not FDA-approved for this condition. Despite the outlook for the patient with lupus improving, the need for more efficacious and safer drugs was well recognised. The twentieth century closed with a foray into clinical trials, but the outcomes of these research efforts were unsuccessful until two positive phase 3 studies with belimumab led to its approval in 2011. Despite the path blazed during the belimumab development program, drug development research in lupus remains quite challenging. The obstacles to drug development are many and relate to the effectiveness of the drug, selection of the correct dose, inclusion of the proper patient population, and the incorporation of appropriate outcome measures, to name just a few. Despite these hurdles, there is currently unprecedented activity in the area of drug development in patients with lupus. The lupus community will overcome these barriers, and no doubt physicians will have more drugs in their armamentarium in the near future.

7 UTILITY OF THE LUPUS LOW DISEASE ACTIVITY STATE (LLDAS) DEFINITION IN DISCRIMINATING RESPONDERS IN THE PHASE IIB MUSE TRIAL OF ANIFROLUMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background and aims LLDAS attainment is associated with reduced organ damage accrual. However, utility of LLDAS as an endpoint has not been evaluated in RCTs. We evaluated LLDAS in a *post-hoc* analysis of the MUSE trial[1] with patients with moderate to severe SLE.

Methods LLDAS requires SLEDAI–2K<4 without major organ activity, no new disease activity, PGA (0–3)<1, prednisolone <7.5 mg/day, and standard immunosuppressant dosage tolerance. LLDAS attainability, association with trial endpoints, and discrimination between anifrolumab- and placebo-treated patients were explored using descriptive statistics, logistic regression, and Grey's test.

Results Patients received intravenous placebo, anifrolumab 300 mg, or 1000 mg in addition to standard of care, every 4 weeks for 48 weeks. LLDAS criteria were met at least once

Abstract 7 Table 1

	Placebo Q4W (N=102)	Anifrolumab 300 mg Q4W (N=99)	Anifrolumab 1,000 mg Q4W (N=104)
LLDAS attainment,[a] n (%)	36 (35)	51 (52)	48 (46)
OR vs. placebo [90% CI]		1.97 [1.19, 3.25]	1.63 [1.00, 2.68]
p value		0.027	0.103
LLDAS attainment for greater than half of the trial duration, n (%)	10 (10)	24 (24)	19 (18)
OR vs. placebo [90% CI]		3.04 [1.53, 6.06]	2.17 [1.07, 4.39]
p value		0.008	0.072
LLDAS attainment at Week 52, n (%)	17 (17)	39 (39)	29 (28)
OR [90% CI]		3.41 [1.93, 6.06]	2.03 [1.13, 3.64]
p value		<0.001	0.046

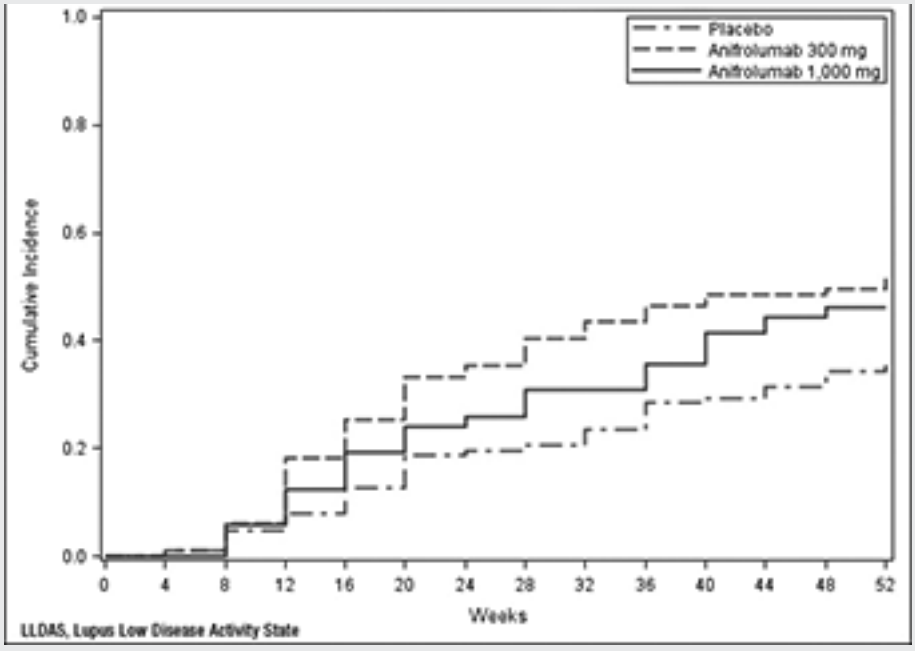
[a]LLDAS criteria met at least once
CI, confidence interval; LLDAS, Lupus Low Disease Activity State; OR, odds ratio; Q4W, every 4 weeks

Abstract 7 Table 2

	SRI(4)[a] response (n=159)	BICLA[a] response (n=121)
LLDAS attainment at Week 52 (n=85[b])		
n	74	62
Within patients in LLDAS, %	87	74
Within outcome responders, %	47	51
χ^2 (*p* value)	57.61 (<0.0001)	55.18 (<0.0001)

[a]Positive association between LLDAS and outcomes seen,
[b]n=84 for BICLA analysis (includes only patients with at least one BILAG A or B at baseline)
BICLA, BILAG-based Composite Lupus Assessment; BILAG, British Isles Lupus Assessment Group; LLDAS, Lupus Low Disease Activity State; SRI, SLE Responder Index

Abstract 7 Table 3



by 35%, 52%, and 46% of patients, respectively (Table 1). At Week 52, LLDAS was associated with key trial outcomes. However, LLDAS was more stringent (Table 2). Treatment with anifrolumab 300 mg and 1000 mg increased LLDAS attainment vs. placebo from Week 12 and Week 28, respectively (OR 300 mg: 1.7–3.6; 1000 mg: 1.7–2.5). LLDAS was achieved more frequently at Week 52 (Table 1), and was attained earlier (300 mg: $\chi^2=6.39$, $p=0.012$; 1000 mg: $\chi^2=2.44$, $p=0.119$) (Figure 1) for anifrolumab vs. placebo.

Conclusions LLDAS correlated with clinically relevant treatment responses, discriminating responders from non-responders. Anifrolumab 300 mg treatment was associated with up to 3.6-fold OR increases of LLDAS attainment. LLDAS should be considered as an endpoint in SLE RCTs.

REFERENCE

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8 EFFICACY AND SAFETY OF ATACICEPT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS OF A 24-WEEK RANDOMISEDRANDOMIZED, PLACEBO-CONTROLLED, PHASE IIB STUDY

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Background and aims Atacicept targets B-cell stimulating factors, BLyS and APRIL. ADDRESS II was a phase IIb, multicenter study (NCT01972568) investigating the efficacy and safety of atacicept in SLE.

Abstract 8 Table 1

	Responder rates (RR), n (%)			Atacicept 75 mg vs placebo			Atacicept 150 mg vs placebo		
	Placebo	Atacicept 75 mg	Atacicept 150 mg	Δ RR	Adjusted OR (95% CI)	p	Δ RR	Adjusted OR (95% CI)	p
*ITT**	*n=100*	*n=102*	*n=104*						
SRI-4 (primary endpoint)[†a]	44 (44.0)	58 (56.9)	56 (53.8)	12.9%	1.71 (0.97–2.99)	0.062	9.8%	1.55 (0.89–2.72)	0.121
SRI-4 (sensitivity analysis)[‡a]	41 (41.0)	57 (55.9)	58 (55.8)	14.9%	1.88 (1.07–3.31)	0.029	14.8%	1.96 (1.11–3.46)	0.020
SRI-6[b]	30 (30.0)	31 (30.4)	38 (36.5)	0.4%	1.03 (0.56–1.89)	0.932	6.5%	1.44 (0.79–2.62)	0.230
ITT SA[#]	*n=29*	*n=29*	*n=26*						
SRI-4[a]	7 (24.1)	17 (58.6)	16 (61.5)	34.5%	5.10 (1.60–16.21)	0.006	37.4%	7.34 (2.09–25.77)	0.002
SRI-6[b]	4 (13.8)	12 (41.4)	12 (46.2)	27.6%	4.80 (1.29–17.81)	0.019	32.4%	6.48 (1.66–25.35)	0.007

*All randomized patients; †screening visit as baseline; ‡pre-specified analysis with study day 1 as baseline; #all patients with positive anti-dsDNA antibodies (≥15 IU/mL) and low complement (C3 <0.9 g/L and/or C4 <0.1 g/L) at baseline (screening visit).

Adjusted OR, 95% CI, and p-values were estimated from a logistic regression model, adjusted for pre-specified covariates.

[a]Improvement in SLEDAI-2K of ≥4 points from baseline, no new BILAG 1A or 2B organ domain flares, no worsening in PGA (<10% increase), and no withdrawal from study or use of prohibited medications during the treatment period; [b]SRI response with improvement in SLEDAI-2K of ≥6 points from baseline (screening visit).

ITT, intention-to-treat; OR, odds ratio; RR, responder rate; SA, serologically active.