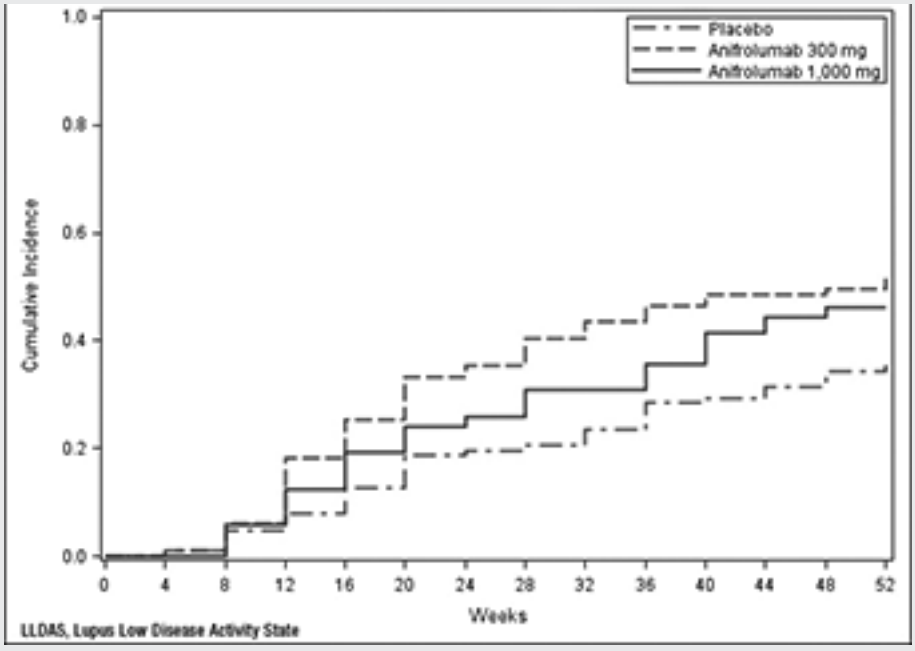
Abstract 7 Table 3



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

[1]JT Merrill*, [2]DJ Wallace, [3]S Wax, [4]A Kao, [5]P Fraser, [4]P Chang, [6]D Isenberg. *[1]Oklahoma Medical Research Foundation, Clinical Pharmacology, Oklahoma, USA; [2]University of California Los Angeles, David Geffen School of Medicine, Los Angeles, USA; [3]EMD Serono Research and Development Institute- Inc, Global Clinical Development Center- Immunology, Billerica, USA; [4]EMD Serono Research and Development Institute- Inc, Global Biostatistics and Epidemiology, Billerica, USA; [5]EMD Serono Research and Development Institute- Inc, Fertility- Immunology and Rheumatology Global Drug Safety Medicine, Billerica, USA; [6]University College London, University College Hospital, London, UK*

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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.

Abstract 8 Table 2

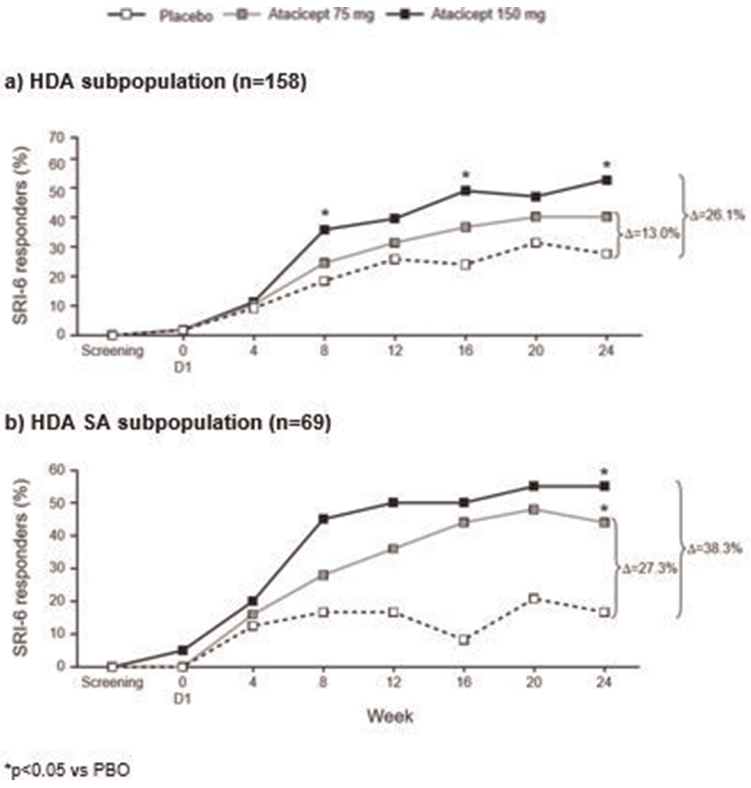
	Responder rates (RR), n (%)			Atacicept 75 mg vs placebo			Atacicept 150 mg vs placebo		
	Placebo	Atacicept 75 mg	Atacicept 150 mg	Δ RR	Adjusted OR (95% CI)	p	Δ RR	Adjusted OR (95% CI)	p
*HDA**	*n=52*	*n=55*	*n=51*						
SRI-4[a]	22 (42.3)	32 (58.2)	32 (62.7)	15.9%	1.95 (0.90–4.23)	0.090	20.4%	2.43 (1.09–5.42)	0.030
SRI-6[b]	15 (28.8)	23 (41.8)	28 (54.9)	13.0%	1.83 (0.81–4.13)	0.143	26.1%	3.30 (1.44–7.59)	0.005
HDA SA†	*n=24*	*n=25*	*n=20*						
SRI-4[a]	6 (25.0)	15 (60.0)	13 (65.0)	35.0%	4.96 (1.43– 17.16)	0.012	40.0%	7.48 (1.84–30.43)	0.005
SRI-6[b]	4 (16.7)	11 (44.0)	11 (55.0)	27.3%	4.12 (1.08– 15.75)	0.038	38.3%	7.13 (1.67– 30.45)	0.008

*All patients with SLEDAI-2K ≥10 at baseline (screening visit); †all patients with SLEDAI-2K ≥10 and 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 (screening visit), 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).

HDA, high disease activity; OR, odds ratio; RR, responder rate; SA, serologically active.

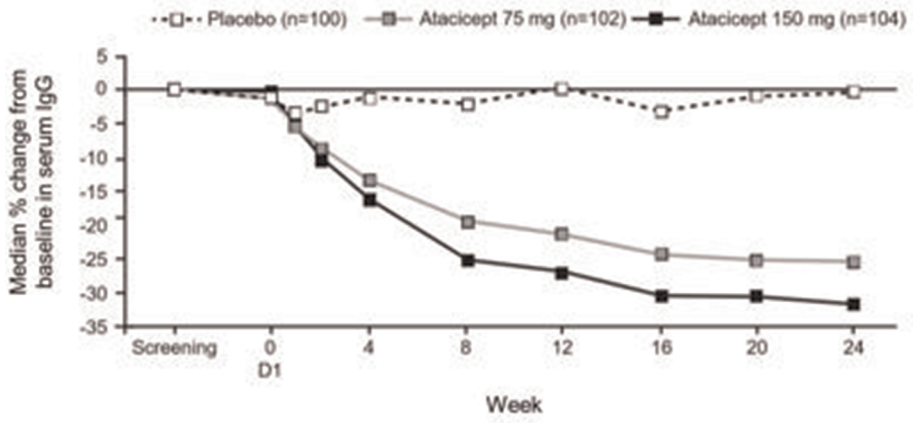


Abstract 8 Figure 1

Abstract 8 Table 3

	Placebo n=100	Atacicept 75 mg n=102	Atacicept 150 mg n=104
Any TEAE, n (%)	71 (71.0)	83 (81.4)	84 (80.8)
Serious TEAEs, n (%)	11 (11.0)	9 (8.8)	6 (5.8)
TEAEs leading to treatment discontinuation, n (%)	6 (6.0)	5 (4.9)	6 (5.8)
Infections and infestations, n (%)	46 (46.0)	45 (44.1)	51 (49.0)
Serious/severe infections and infestations, n (%)	7 (7.0)	9 (8.8)	1 (1.0)
Deaths, n (%)	0 (0.0)	0 (0.0)	0 (0.0)

TEAE, treatment-emergent adverse events



Abstract 8 Figure 2

Methods Patients with active (SLEDAI-2K≥6), autoantibody-positive SLE receiving standard therapy were randomised to weekly subcutaneous injections of atacicept (75 or 150 mg) or placebo for 24 weeks.
Results In the ITT population (n=306), there was a trend towards improved SRI-4 response rates with both atacicept doses vs placebo at Week 24 (primary analysis, Screening as baseline). In a sensitivity analysis using Day 1 as baseline, both atacicept doses significantly increased SRI-4 responses (Table 1). In patients with high disease activity (HDA, n=158), serologically active (SA) disease (n=84), or both (HDA SA, n=69), enhanced improvements in SRI-4 and SRI-6 response rates were seen with atacicept (Tables 1 and 2; Figure 1). Atacicept significantly reduced severe flares in the ITT (75 mg: BILAG A p=0.019; 150 mg: SLEDAI flare index [SFI] p=0.002) and HDA populations (75 mg: BILAG A HR=0.1, SFI HR=0.3; 150 mg: BILAG A HR=0.3, SFI HR=0.2; all p<0.05). At Week 24, serum IgG was reduced from baseline by ~25% and ~30% with atacicept 75 and 150 mg, respectively (Figure 2); serum complement C3 and C4 increased while IgM, IgA, and anti-dsDNA antibodies decreased with atacicept. Risk of SAEs and serious/severe infections did not increase with atacicept (Table 3).
Conclusions Atacicept demonstrated evidence of efficacy in SLE, particularly in HDA and SA patients, with reduction in disease activity and severe flares, and showed a favourable safety profile.

Plenary Session 4: Cutting edge science in SLE

9 BIM SUPPRESSES THE DEVELOPMENT OF SLE BY LIMITING MACROPHAGE INFLAMMATORY RESPONSES

H Perlman*, F Tsa, C Cuda, P Homan, D Winter. *Northwestern University, Medicine, Chicago, USA*

10.1136/lupus-2017-000215.9

Background and aims There are numerous endogenous Bcl-2 antagonists that share similar homology, structure, topology and expression pattern, yet only the loss of Bim in mice is sufficient to lead to the development of a systemic autoimmunity.
Methods We investigated the contribution of Bim in monocytes/macrophages and its effect on systemic autoimmunity by establishing conditionally Bim-deleted mice in the monocyte/macrophage compartment ($Cre^{LysM}Bim^{fl/fl}$ mice) and examined the development of lupus-like disease over time.
Results Patients with lupus display decreased expression of Bim in circulating monocytes and reduced Bim expression in kidney macrophages. $Cre^{LysM}Bim^{flox/flox}$ mice develop a lupus-like disease that mirrors aged $Bim^{-/-}$ mice including loss of the marginal zone macrophages, splenomegaly, lymphadenopathy, autoantibodies including anti-DNA IgG, and a type I interferon signature as compared to control mice. $Cre^{LysM}Bim^{flox/flox}$ mice also exhibit increased mortality attributed to immune complex deposition and increased numbers of kidney macrophages all of which contribute to glomerulonephritis. The loss of Bim in macrophages is sufficient to break tolerance as adoptive transfer of wild-type lymphocytes into $Cre^{LysM}Bim^{flox/flox}$-$Rag^{-/-}$ mice leads to systemic autoimmunity. We also identified that the loss of TLR signalling adaptor protein TRIF but not MyD88 is essential for progression to GN phase but is dispensable for systemic autoimmunity. RNA seq analysis of sorted kidney macrophages revealed a novel Bim and lupus specific signatures.
Conclusions These data add another facet to the conventional dogma that Bim's central role in autoimmune disease is to prevent the escape of autoreactive lymphocytes from apoptosis. Thus, Bim may be a novel therapeutic target for treating SLE.

10 SINGLE CELL EXPRESSION QUANTITATIVE TRAIT LOCI (EQTL) ANALSIS OF ESTABLISHED LUPUS-RISK LOCI IN PATIENT MONOCYTES

[1]Y Ghodke-Puranik, [1]J Zhongbo, [2]W Fan, [1]M Jensen, [1]J Dorschner, [1]D Vsetecka, [1]S Amin, [1]A Makol, [1]F Ernste, [1]T Osborn, [1]K Moder, [1]V Chowdhary, [1]T Niewold*. *[1]Mayo Clinic, Division of Rheumatology and Department of Immunology, Rochester, USA; [2]Ren Ji Hospital- Shanghai Jiao Tong University, School of Medicine- Department of Rheumatology, Shanghai, China*

10.1136/lupus-2017-000215.10

Background and aims While most of the confirmed SLE-risk loci are in or near genes with immune system function, a major unanswered question is how these loci influence diverse immune cell subsets.
Methods CD14++CD16- classical monocytes (CL) and CD14dimCD16+ non classical (NCL) monocytes from SLE patients were purified by magnetic separation. The Fluidigm C1 System was used for single cell capture and target gene pre-amplification and equal numbers of classical and non-