corresponding with decreased expression of related chemokines IP-10, Mig, and RANTES in the kidney. The proportion of macrophage and neutrophil cells and related chemokines expression was also reduced in kidneys of LLDT-8-treated mice. In the human proximal tubule epithelial cell line and mouse mesangial cell line, consistent with our in vivo experimental results, LLDT-8 suppressed the expression of related chemokines and IL-6.

Conclusions In summary, LLDT-8 has a therapeutic benefit for lupus nephritis via suppressing chemokine expression and inhibiting immune cell infiltration in kidneys of MRL/lpr mice.

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209 ATTAINMENT OF LOW DISEASE ACTIVITY AND REMISSION WITH ATACICEPT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND HIGH DISEASE ACTIVITY IN THE PHASE IIB ADDRESS II STUDY AND ITS LONG-TERM EXTENSION

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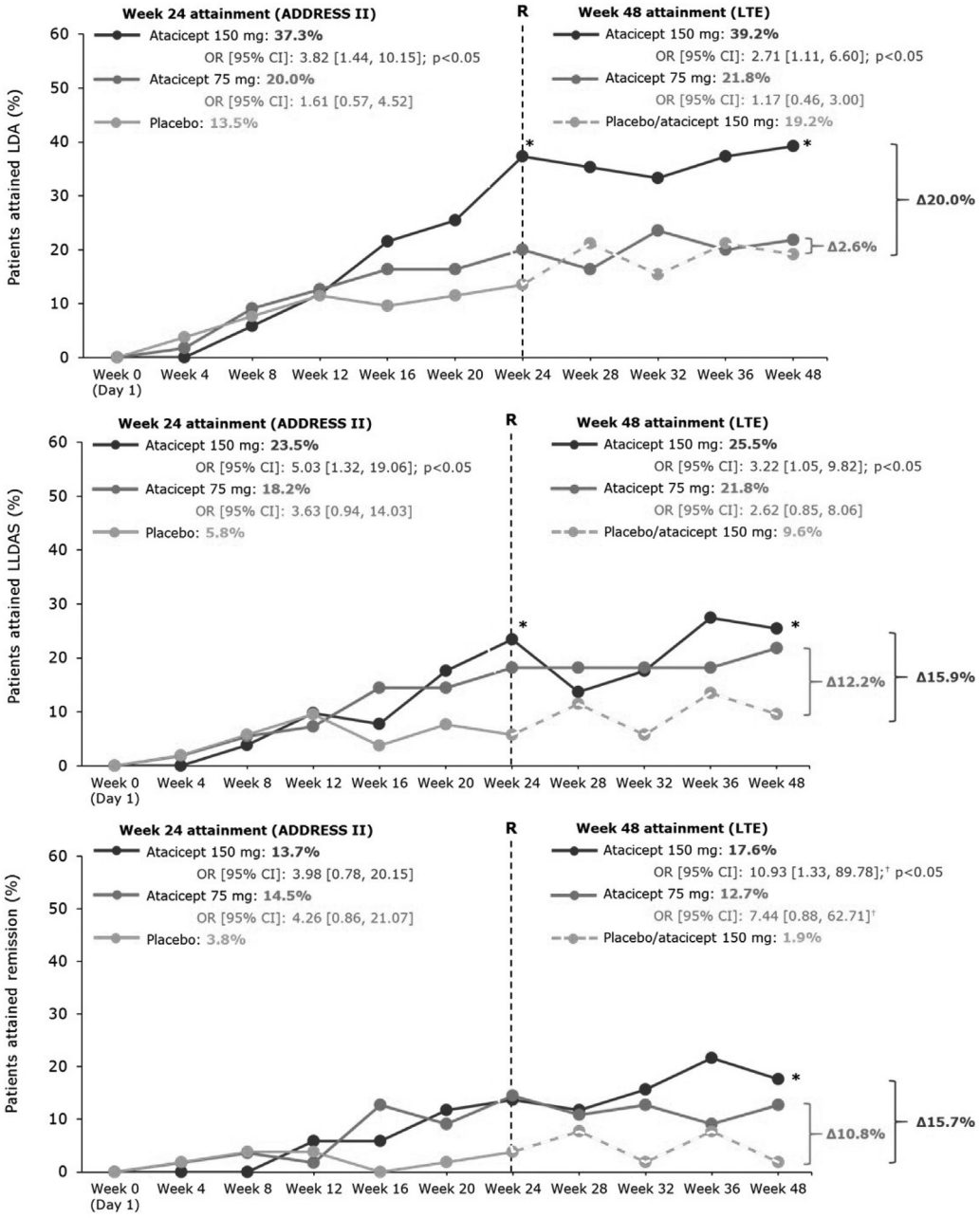

*p<0.05 versus placebo (24 weeks) or placebo/atacicept 150 mg (48 weeks); †Results should be interpreted with caution due to the wide CI; **CI,** Confidence interval; **LDA,** Low disease activity; **LLDAS,** Lupus Low Disease Activity State; **LTE,** Long-term extension; **OR,** Odds ratio

Abstract 209 Figure 1

Background Low disease activity (LDA) and remission are important goals in the treatment of patients with SLE.[1 2] Lupus Low Disease Activity State (LLDAS) is associated with reduced damage accrual,[2] and has been shown to be a feasible clinical trial endpoint.[3] In patients with high disease activity (HDA; SLEDAI-2K ≥10) enrolled in the ADDRESS II study, atacicept improved SLE responder index (SRI)-6 response rates and flare prevention at Week 24 vs placebo. Atacicept also demonstrated an acceptable safety profile.[4] We present a post-hoc analysis of data from ADDRESS II and its long-term extension, describing 48-week LDA and remission rates in patients with HDA at Screening.

Methods In ADDRESS II, patients were randomized (1:1:1) to weekly subcutaneous atacicept 75 or 150 mg or placebo for 24 weeks. Atacicept-completers continued at the same dose in the extension study, while placebo-treated patients were switched to atacicept 150 mg (placebo/atacicept 150 mg). This post-hoc analysis assessed: LDA (SLEDAI-2K ≤2), LLDAS (SLEDAI-2K ≤4 without major organ activity, no new disease activity vs previous visit, Physician's Global Assessment [PGA] ≤1, prednisone-equivalent ≤7.5 mg/day, and stable immunosuppressants),[2] and remission (clinical SLEDAI-2K=0, PGA <0.5, prednisone ≤5 mg/day), as proposed by the task force on definitions of remission in SLE (DORIS).[1]

Results Of 306 ADDRESS II patients, 158 (51.6%) had HDA at Screening. At Week 24, 42.4% achieved SRI-6, 23.4% attained LDA, 15.8% LLDAS and 10.8% remission. At Week 48, 52.5% achieved SRI-6, 26.6% attained LDA, 19.0% LLDAS and 10.8% remission. Among 83 patients with HDA at Screening who had an SRI-6 response at Week 48, 49.4% (n=41) attained LDA, 34.9% (n=29) LLDAS and 20.5% (n=17) remission. At 48 weeks, LDA, LLDAS and remission rates were higher in patients treated with atacicept 150 mg vs atacicept 75 mg and vs placebo/atacicept 150 mg (figure 1).

Conclusions ADDRESS II patients with HDA at Screening who received atacicept 150 mg were more likely to attain LDA, LLDAS and remission at Week 48 than those treated with atacicept 75 mg or placebo/atacicept 150 mg. These endpoints were more stringent and discriminatory than SRI-6, confirming LLDAS, LDA, and remission to be robust and meaningful endpoints for SLE trials. In addition, these data further support future studies of atacicept in SLE.

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REFERENCES

1. Van Vollenhoven *et al. Ann Rheum Dis* 2017.
2. Franklyn *et al. Ann Rheum Dis* 2016.
3. Morand *et al. Ann Rheum Dis* 2018.
4. Merrill *et al. Arthritis Rheum* 2018.

210 INTEGRATED SAFETY PROFILE OF ATACICEPT FROM ALL CLINICAL STUDIES TO DATE

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Background We conducted an integrated analysis of pooled safety data from all 17 atacicept clinical studies across

Abstract 210 Table 1 Exposure-adjusted TEAE rates by dose (DBPC set)

		Atacicept				
	Placebo, n=483	**25 mg, n=129**	**75 mg, n=384**	**150 mg, n=572**	**All, n=1085**	**Total, n=1568**
Total number of patient-years	278.3	51.5	225.0	286.7	563.2	841.4
TEAE, n (per 100 patient-years)						
Hypersensitivity*	37 (13.9)	8 (15.7)	40 (19.1)	55 (20.4)	103 (19.4)	140 (17.6)
Infections	211 (107.8)	43 (104.4)	180 (118.7)	281 (141.3)	504 (128.7)	715 (121.7)
Herpes zoster	13 (4.7)	2 (3.9)	10 (4.5)	17 (6.1)	29 (5.2)	42 (5.1)
Serious infection	20 (7.3)	1 (1.9)	23 (10.5)	22 (7.7)	46 (8.3)	66 (7.9)
Severe infection	9 (3.2)	0	11 (4.9)	16 (5.6)	27 (4.8)	36 (4.3)
Injection site reactions	54 (20.9)	27 (64.8)	109 (63.0)	156 (72.4)	292 (67.9)	346 (50.2)
Severe hypogammaglobulinemia (IgG <3 g/L)	0	0	2 (0.9)	4 (1.4)	6 (1.1)	6 (0.7)
Cardiac arrhythmias [all]*	18 (6.6)	11 (22.4)	23 (10.6)	25 (8.9)	59 (10.8)	77 (9.4)
Ventricular arrhythmias	5 (1.8)	0	4 (1.8)	6 (2.1)	10 (1.8)	15 (1.8)
Ischemic heart disorders*	11 (4.0)	3 (5.9)	13 (5.9)	11 (3.9)	27 (4.9)	38 (4.6)
Embolic and thromboembolic events*	11 (4.0)	1 (2.0)	6 (2.7)	9 (3.2)	16 (2.9)	27 (3.2)
Vestibular disorders*	19 (7.0)	5 (9.9)	18 (8.3)	26 (9.3)	49 (8.9)	68 (8.3)
Demyelination*	1 (0.4)	1 (1.9)	0	5 (1.7)	6 (1.1)	7 (0.8)
Depression*	14 (5.1)	3 (5.8)	8 (3.6)	11 (3.9)	22 (3.9)	36 (4.3)
Malignant tumor*	0	1 (1.9)	1 (0.4)	3 (1.1)	5 (0.9)	5 (0.6)
Serious TEAE	51 (18.9)	15 (30.0)	51 (23.9)	61 (21.8)	127 (23.4)	178 (21.9)
Severe TEAE	28 (10.2)	10 (19.6)	45 (20.9)	56 (20.0)	111 (20.3)	139 (17.0)
Discontinuation of treatment due to TEAE	30 (10.9)	14 (27.6)	30 (13.4)	46 (16.1)	90 (16.1)	120 (14.3)
Deaths related to infections, n (%)						
Deaths	0	0	0	2 (0.3)†	0	0

*Programmatically determined (crude results of the search) from a predefined list of MedDRA preferred terms according to the Standardized MedDRA Query (SMQ) or Customized MedDRA Query (CMQ) classification of the corresponding MedDRA version
†Acute respiratory failure and probable leptospirosis (n=1); pneumonia and pulmonary alveolar hemorrhage (n=1)