S7a – New therapeutic candidates

S7A:4 REDUCTION OF SYSTEMIC LUPUS FLARES BY ATACICEPT IN A RANDOMISED, PLACEBO-CONTROLLED, PHASE IIB STUDY (ADDRESS II) AND ITS EXTENSION STUDY

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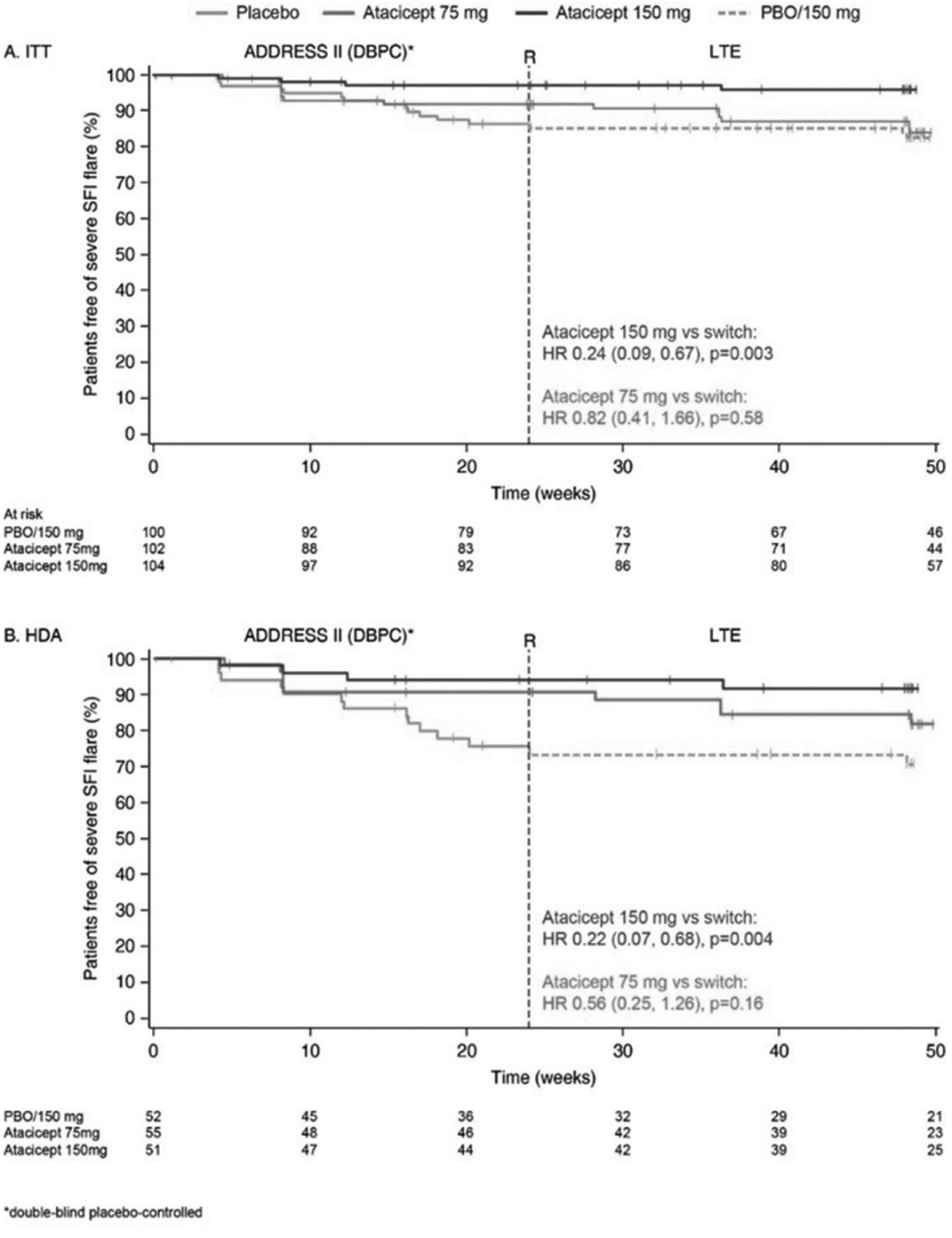
Purpose Atacicept targets the B-cell stimulating factors, BLyS and APRIL, and has shown evidence of clinical response in patients with SLE. The 24 week Phase II ADDRESS II (NCT01972568) Study and its long-term extension (LTE; NCT02070978) provided data on disease activity with up to 48 weeks of atacicept treatment.

Methods In ADDRESS II, patients were randomised (1:1:1) to receive weekly atacicept (75 or 150 mg SC injection) or placebo (PBO) for 24 weeks. Those who completed treatment were eligible to enter the LTE, to either continue on the same atacicept dose (atacicept groups), or switch from PBO to atacicept 150 mg (PBO/150 mg). The SLE flare analysis from both studies are reported here.



Abstract S7A:4 Figure 1

Results The ITT population of ADDRESS II included 306 patients; 158 of whom met the predefined high disease activity (HDA) criterion (SLEDAI-2K≥10 at Screening). Of the 262 patients who completed the ADDRESS II, 253 entered the LTE. At 24 weeks in the PBO-controlled trial, cumulative incidence of severe flare was significantly reduced with atacicept 75 mg vs PBO by BILAG A (HR 0.24; p=0.0186), and with atacicept 150 mg vs PBO by SFI (HR 0.18; p=0.002). There was no difference in moderate-to-severe flare by BILAG A/2B. In the HDA subpopulation, incidence of severe flare at 24 weeks was significantly reduced with both atacicept doses vs PBO by BILAG A (75 mg HR 0.08, p=0.002; 150 mg HR 0.32, p=0.038) and SFI (75 mg HR 0.33, p=0.029; 150 mg HR 0.19, p=0.004). Incidence of moderate-to-severe flare by BILAG A/2B was significantly reduced with atacicept 150 mg vs PBO (HR 0.34, p=0.032). At 48 weeks, risk of severe flare by SFI was significantly lower with atacicept 150 mg vs the PBO/150 mg in both the ITT and HDA populations (figure 1); significant flare reductions were seen with atacicept 75 mg by BILAG A, and with both atacicept doses by BILAG A/2B vs PBO/150 mg, in the HDA subpopulation.

Conclusions In this 24 week, double-blind, PBO-controlled trial, atacicept treatment was associated with significant flare reductions compared with PBO. Rates of flare continued to be low in atacicept-treated patients between weeks 24–48. Most flares occurred in HDA patients in the PBO group.

S7A:5 SRI RESPONSE, ATTAINMENT OF LOW DISEASE ACTIVITY AND SAFETY IN PATIENTS WITH SYSTEMIC LUPUS TREATED WITH ATACICEPT IN A PHASE IIB STUDY (ADDRESS II)

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Purpose Atacicept targets B-cell stimulating factors, BLyS and APRIL. ADDRESS II (NCT01972568) investigates the efficacy and safety of atacicept in SLE.

Methods In this Phase IIb multicenter study, patients with active (SLEDAI-2K≥6), autoantibody-positive SLE on standard of care therapy received weekly SC injections of atacicept (75 or 150 mg) or placebo (PBO) for 24 weeks. The primary endpoint was proportion of patients achieving SLE responder index (SRI)−4 response at week 24. Other endpoints included SRI-5 through SRI-8 response and low disease activity (LDA) attainment, defined as LDA-1 (SLEDAI-2K≤2), LDA-2 (SLEDAI-2K≤2 and prednisone-equivalent ≤7.5 mg/day), or LLDAS (SLEDAI–2K≤4 without major organ activity, no new disease activity vs previous visit, Physician's Global Assessment≤1,

Abstract S7A:5 Table 1 Clinical response endpoints at week 24 for the HDA subpopulation

	PBO	Atacicept 75 mg	Atacicept 150 mg
	n=52	n=55	n=51
SRI response, n (%)			
SRI-4	22 (42.3)	33 (60.0)	32 (62.7)*
SRI-5	15 (28.8)	24 (43.6)	28 (54.9)†
SRI-6	15 (28.8)	24 (43.6)	28 (54.9)†
SRI-7	11 (21.2)	20 (36.4)	22 (43.1)*
SRI-8	11 (21.2)	19 (34.5)	22 (43.1)*
LDA			
LDA-1, n (%)	7 (13.5)	11 (20.0)	19 (37.3)
OR (95% CI)		1.61 (0.57, 4.52)	3.82 (1.44, 10.15) †
LDA-2, n (%)	4 (7.7)	4 (7.3)	11 (21.6)
OR (95% CI)		0.94 (0.22, 3.98)	3.30 (0.98, 11.17)
LLDAS, n (%)	3 (5.8)	10 (18.2)	12 (23.5)
OR (95% CI)		3.63 (0.94, 14.03)	5.03 (1.32, 19.06)*

CI, confidence interval; LDA, low disease activity; LLDAS, Lupus low disease activity state; OR, odds ratio; PBO, placebo; SLE, systemic lupus erythematosus; SRI, SLE responder index
LDA-1: SLEDAI-2K ≤2
LDA-2: SLEDAI-2K ≤2 and Prednisone-equivalent ≤7.5 mg/day
LLDAS: SLEDAI–2K ≤ 4 without major organ activity, no new disease activity compared with previous visit, Physician's Global Assessment (0–3) ≤1, prednisone-equivalent ≤7.5 mg/day, and stable maintenance doses of immunosuppressants
*p<0.05; †p<0.01