Effect of Atacicept on Renal Function in SLE Patients

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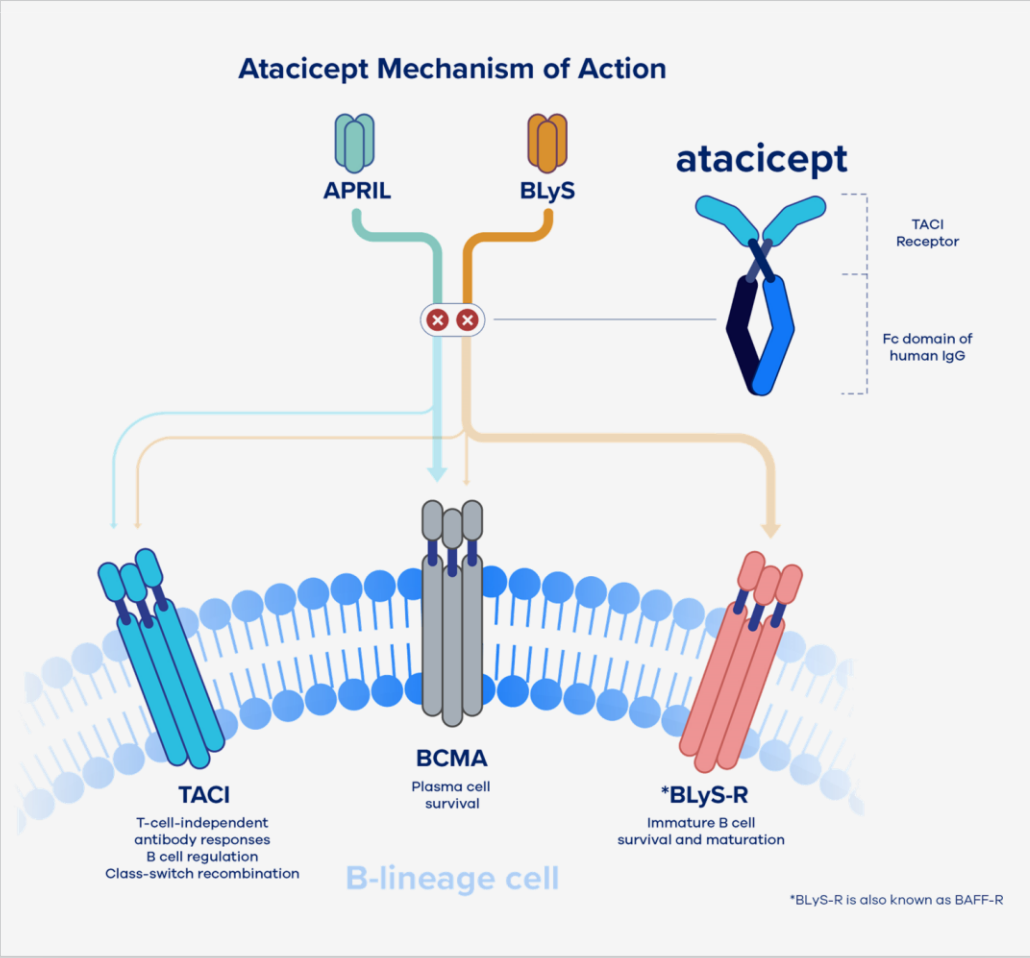
Disclosures

- David Isenberg: Consultant for Vera Tx, Servier, AstraZeneca, Idorsia, EMD Serono, and Amgen. His honoraria are passed onto a local arthritis charity
- Celia J.F. Lin: Employee of Vera Therapeutics
- Amy Kao: Own stocks and employee of EMD Serono Research & Development Institute, Inc (a business of Merck KGaA)
- Aida Aydemir: Employee of EMD Serono Research & Development Institute, Inc (a business of Merck KGaA)
- Caroline Gordon: Speakers bureau for UCB, Consultant for the Center for Disease Control and Prevention, Amgen, Astra-Zeneca, AbbVie, EMD Serono, MGP, Sanofi, and UCB. Educational grant from UCB to Sandwell and West Birmingham Hospitals NHS Trust that supported previous research work unrelated to any specific drug (last payment July 2019)

Atacicept is a Dual Inhibitor (BLyS and APRIL) of Plasma Cells and B Cells



Key Considerations

- Fully humanized fusion protein, subcutaneously administered weekly
- Dual blockade by TACI-Ig shown to be more potent than blocking BLyS alone or APRIL alone[1] and has benefit of targeting long-lived plasma cells[2], in addition to B cells, thus reducing autoantibody production[3]

[1] Haselmayer P et al. Eur J Immunol 2017;00:1–11. [2]Hiepe F et al. Nat Rev Rheumatol 2011;3:170-178. [3]Gordon et al. 2017 Arthritis & Rheumatology 69(1): 122-130.

Atacicept demonstrated clinical efficacy in SLE, with a delayed time to first flare in treated patients compared to placebo

APRIL-SLE Trial Design	
Multicenter, double-blind, placebo-controlled, randomized, dose-ascending study	
Trial Population	Patients (n=461) with active SLE[1]
Dosing	• Subcutaneous injection • Randomized to atacicept 75 or 150 mg or placebo • Twice-weekly dosing for four weeks, then weekly dosing for 48 weeks

[1] Defined as y category A or B manifestations (excluding a single B score in haematology) on the BILAG index. [2] Defined as BILAG flare score A or B. Source: Isenberg, D, Gordon C, Licu D, et al. Ann Rheum Dis. 2015 Nov; 74(11):2006-15.

Primary endpoint not met for atacicept 75 mg; however, ad hoc analysis showed treatment benefit of atacicept 150 mg in prevention of flare

Proportion of Subjects Who Experienced a Flare in the 52-Week Treatment Period by Analysis Population in APRIL-SLE

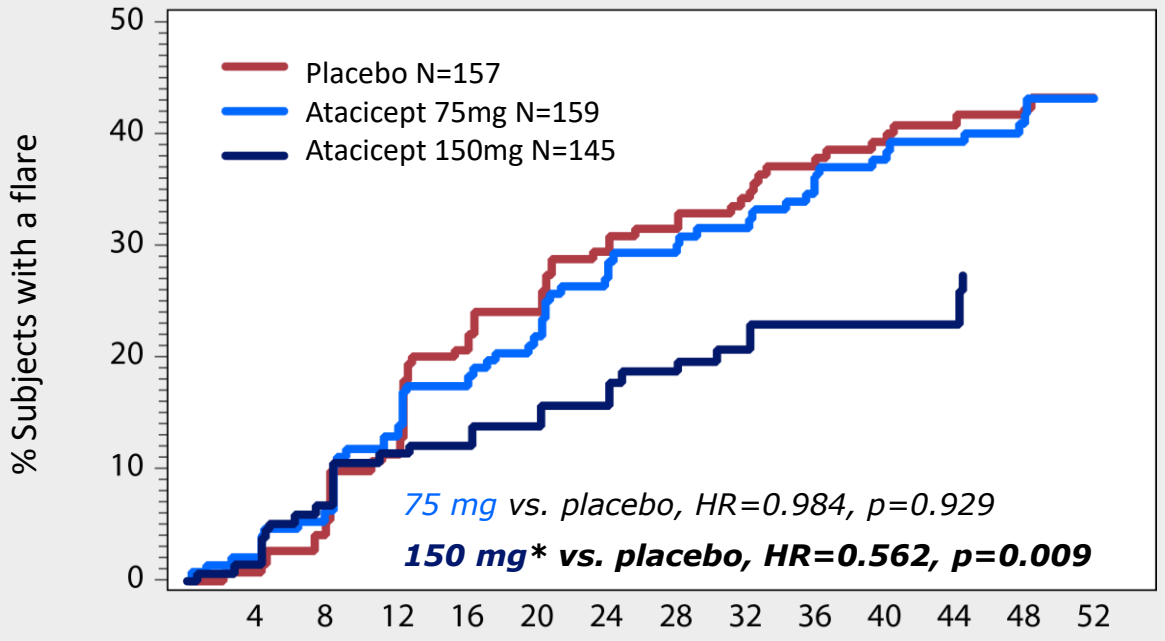
Population	Statistic	Placebo	Atacicept 75 mg	Atacicept 150 mg
mITT	n Presence of a flare, n (%) Odds Ratio[a] [95% CI] p-value	154 82 (53.25)	157 90 (57.32) 1.160 [0.74, 1.82] 0.518	144 52 (36. 11) 0.490 [0.31, 0.78] 0.003
PC	n Presence of a flare, n (%) Odds Ratio[a] [95% CI] p-value	81 49 (60.49)	84 49 (58.33) 0.893 [0.48, 1.67] 0.724	81 35 (43.21) 0.491 [0.26, 0.92] 0.027

Source: Study 27646 CSR Tables 15.2.1.1a, Table 15.2.1.1b, Table 15.2.1.1c, Table 15.2.1.1d
CI= confidence interval; mITT = modified Intent-to-Treat (all randomized and treated subjects); PC= potential completer (all randomized and treated subjects who were randomized at least 52 weeks before discontinuation of the atacicept 150 mg group, and who therefore had the opportunity to complete the 52-week treatment period before this treatment group was discontinued).
[a] Odds ratios were calculated from a logistic regression model adjusted for race and disease severity reported at Screening. Race and disease severity were not statistically significant in the model.

The APRIL-SLE study associated atacicept with a delayed time to first new flare and fewer subjects with corticosteroid increase

APRIL-SLE Trial Findings

Time to First Flare in mITT



% Subjects with Corticosteroid Increase in Potential Completers*

Treatment Group	Any Increase in Steroid	≥20 mg Increase in Prednisone (High Dose)
Placebo	35.6%	32.1%
Atacicept 75 mg	29.8%	27.4%
Atacicept 150 mg	13.6%	12.3%

Key APRIL-SLE Trial Findings

Post-hoc analyses found:

- Atacicept demonstrated flare prevention, with a **reduced proportion of subjects with flare with 150 mg vs placebo**
- **Delayed time to first new flare** observed with atacicept 150 mg vs placebo
- Atacicept was associated with **fewer subjects with corticosteroid increase**

Source: Isenberg, D, Gordon C, Licu D, et al. Ann Rheum Dis. 2015 Nov; 74(11):2006-15

Objective

We performed a post hoc analysis to describe the effect of atacicept compared to placebo on measures of renal function in patients with SLE

Methods

APRIL-SLE study excluded moderate to severe GN, as defined by either of the following:

- urinary protein/creatinine ratio (UPCR) > 1 mg/mg and/or hematuria or
- a significant renal impairment as defined by estimated glomerular filtration rate (eGFR) < 50 mL/min/1.73 m^2

UPCR and eGFR were measured at baseline, week 2, and then every 4 weeks until week 52

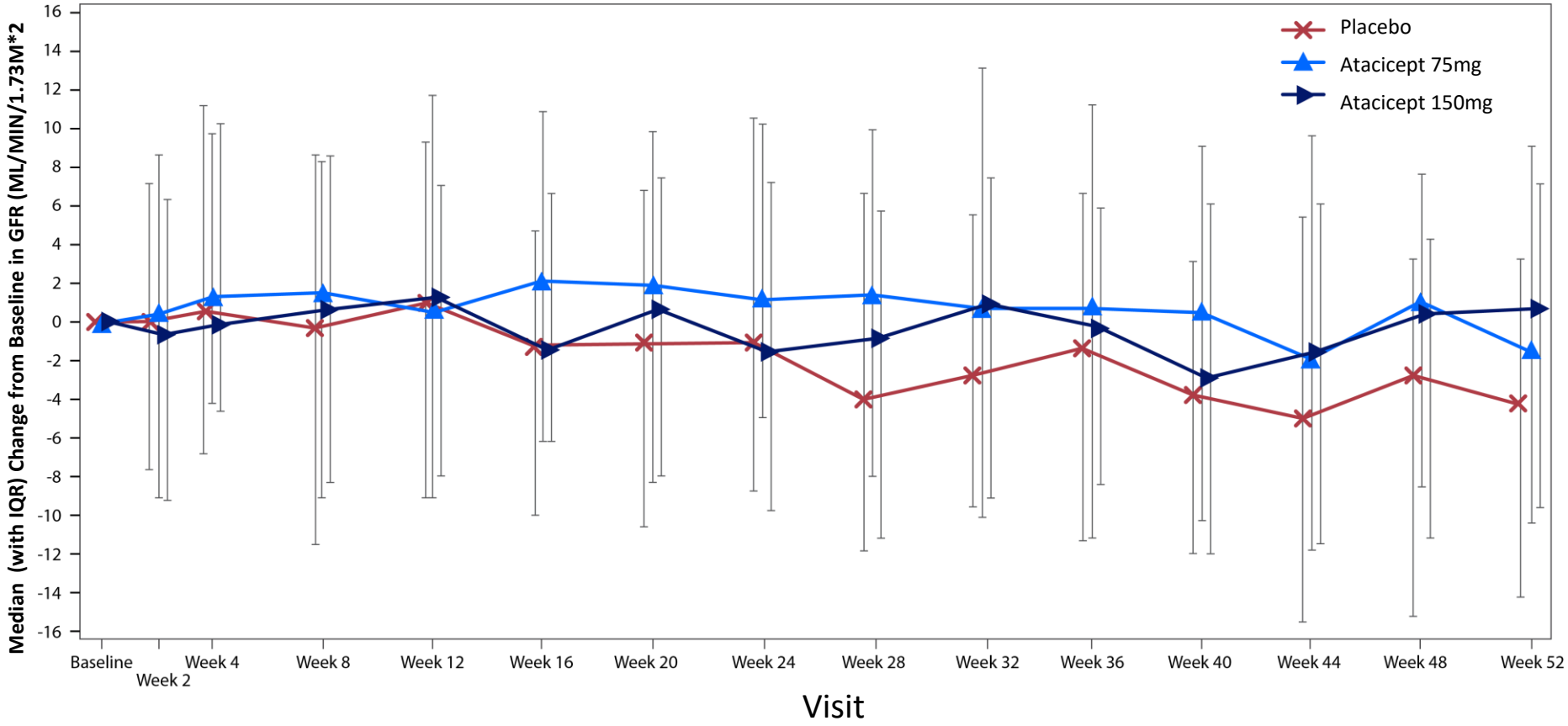
Results

- 111 patients in the placebo group, 112 patients in the atacicept 75 mg group, and 62 patients in the atacicept 150 mg group completed 52 weeks of treatment with eGFR and UPCR analyses

- Estimated GFR showed stability for the atacicept groups compared to an absolute median change from baseline decline of 4.35 in the placebo group at week 52

- UPCR from baseline at week 52 declined in the atacicept groups and increased in the placebo group

Median Change from Baseline in eGFR showed stability for the atacicept groups compared to decline in placebo at week52



Placebo	N=153	148	149	147	142	143	139	138	131	128	128	123	115	110	110
Atacicept 75mg	N=155	147	143	139	136	133	132	125	121	123	116	116	113	111	111
Atacicept 150mg	N=144	141	141	127	122	116	107	100	97	90	85	78	68	70	62

GFR = glomerular filtration rate; SLE = systemic lupus erythematosus

In addition to eGFR trends favorable for atacicept, UPCR declined in atacicept groups and increased in the placebo group at Week 52

Variable	Placebo	Atacicept 75 mg	Atacicept 150 mg
eGFR (mL/min)	n=110	n=111	n=62[b]
median	-4.35	-1.49	0.57
UPCR (mg/mg)	n=108	n=108	n=63
median	6.29	-6.27	-12.72
UPCR (mg/mg)[a]	n=12	n=15	n=8
median	26.11	-54.42	-12.15

eGFR=estimated glomerular filtration rate; UPCR=urinary protein/creatinine ratio
a Among patients with screening UPCR ≥0.2 mg/mg
b Enrollment in the atacicept 150 mg arm was discontinued prematurely (described in Isenberg et al., 2015)

Conclusion

Results from this double-blind, placebo-controlled, Phase 2 study (APRIL-SLE) suggest a **potential for improved renal function with atacicept treatment of patients with moderate-to-severe SLE**, which included patients with proteinuria with proteinuria and mild-moderate chronic kidney disease, as assessed by KDIGO criteria

The ongoing **Phase 3 COMPASS trial evaluating atacicept 150 mg in lupus nephritis** will determine the efficacy and safety of atacicept in moderate to severe active lupus renal disease

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