Atacicept Reduces Serum Immune Complex Levels in Patients with Immunoglobulin A Nephropathy (IgAN)

Jonathan Barratt[1], Celia J. Lin[2], Nadia Nawaz[1], Karen Molyneux[1], Gerald B. Appel[3], James A.Tumlin[4], Yusuke Suzuki[5]
1. University of Leicester, Leicester, Leicestershire, United Kingdom. 2. Vera Therapeutics, Inc, Brisbane, CA, United States 3. Columbia University Medical Center, New York, NY, United States. 4. Emory University School of Medicine, Atlanta, GA, United States. 5. Juntendo University Faculty of Medicine, Tokyo, Japan.

Abstract #: 3770024

Background:

- IgAN is an autoimmune disease with a 4-hit mechanism that results in the inflammatory pathogenic process.
  - Elevated serum galactose-deficient IgA1 (Gd-IgA1), which plays a central role in IgAN pathogenesis is the first hit.
  - The second hit is the production of anti-Gd-IgA1 antibodies leading to formation of immune complexes (third hit).
  - These circulating immune complexes can then deposit in the glomerulus and cause injury (fourth hit).
- The Ph2a JANUS trial showed that atacicept was the first therapeutic to decrease both circulatory Gd-IgA1 and anti-Gd-IgA1 in a RCT of IgAN patients. This analysis investigated whether atacicept can also reduce serum immune complex levels.

Methods:

JANUS patients were evaluated for serum IgA-IgG immune complex levels by ELISA at baseline, weeks 4, 12, 24, 48, and 72. Serum samples were normalized using 3 standard serum samples included on all plates.

Results:

- Decrease in serum IgA-IgG immune complex levels was observed in both atacicept 25 mg and 75 mg groups over time.
- At 24 weeks, mean percent change from baseline was 17% decrease for atacicept 25 mg, 21% decrease for atacicept 75 mg, and 3% decrease for placebo.
- At 72 weeks, 29% decrease for atacicept 25 mg, 26% decrease for atacicept 75 mg, and 13% decrease for placebo was observed.

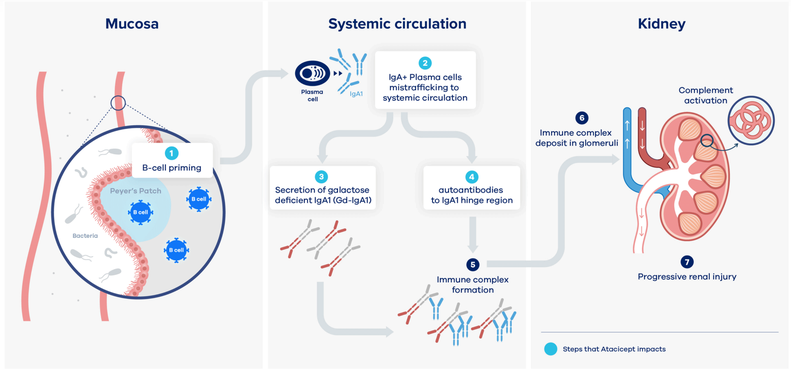

Figure 1: Pathogenesis of IgA Nephropathy

Atacicept Lowers Immune Complexes

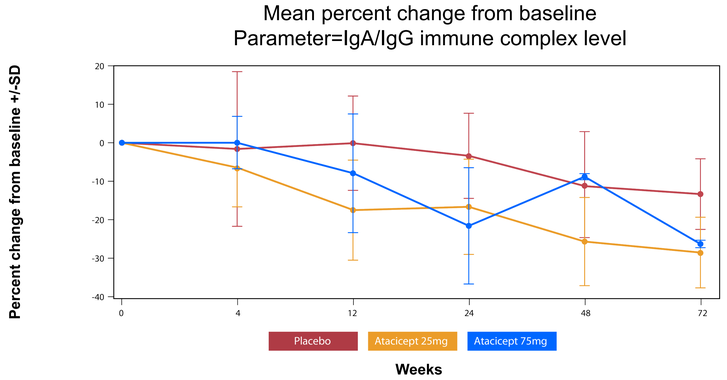

Figure 2: Percent change from baseline in immune complexes to week 72

Atacicept lowers Gd-IgA1

- In the JANUS randomized, placebo-controlled trial in IgAN patients, atacicept, administered subcutaneously once weekly, demonstrated a substantial reduction in serum Gd-IgA1 in a dose dependent manner that was durable through 72 weeks.
- The largest effect was seen in the atacicept 75 mg arm, where after 24 weeks all subjects had reductions in serum Gd-IgA1 to the lowest quartiles, which is associated with the most favorable renal survival.

Atacicept lowers anti-Gd-IgA1

- Data from the same trial demonstrated decrease in serum anti-Gd-IgA1 levels observed in both atacicept 25- and 75-mg groups over time. At 24 weeks, mean % change from baseline was 24% decrease for atacicept 25 mg and 29% decrease for atacicept 75 mg. At 72 weeks, 28% decrease for atacicept 25 mg and 39% decrease for atacicept 75 mg was observed.

Conclusion:

- Atacicept is the first therapeutic to show reduction in serum Gd-IgA1, anti-Gd-IgA1, and now immune complex levels in IgAN patients.
- Atacicept's ability to mitigate the first three hits of the 4-hit mechanism illustrates its potential as a disease-modifying treatment for IgAN.
- The ongoing Ph2b ORIGIN trial evaluating atacicept 25 mg, 75 mg, and 150 mg in IgAN patients will help determine how attenuation of these multiple hits translates to preservation and improvement of renal function.

vera therapeutics

Sources: Study MS700461-0035 CSR Tables 15.3.3.35; Barratt, et al. Kid Int Rep. 2022 (7), 1831-1841.