Atacicept Reduces Hematuria and Serum Gd-IgA1, Both Associated with Long-Term Renal Outcomes in IgAN: 36 Week Results from the Phase 2b ORIGIN Study


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Introduction

• IgA nephropathy (IgAN) is the most common primary glomerulonephritis and a significant contributor to ESRD worldwide.1,2

• Hematuria is an indicator of IgAN activity representing active glomerulonephritis and resolution is associated with improved renal outcomes.3-5

• Elevated serum levels of Gd-IgA1 are recognized as an autoantigen by anti-Gd-IgA1 autoantibodies, forming immune complexes that lead to renal damage in IgAN.6

• High Gd-IgA1 levels are associated with greater risk of renal function deterioration, ESRD, and death.7

Atacicept: Dual BAFF/APRIL Inhibitor

• Atacicept is a fully humanized fusion protein composed of TACI, a native receptor for BAFF and APRIL, and the Fc portion of IgG, in clinical development for weekly subcutaneous self-administration at home.

• The Phase 2b ORIGIN study, a randomized, double-blind, placebo-controlled clinical trial evaluating atacicept in IgAN, met its primary endpoint:

- Week 36 results showed a similar safety profile between atacicept and placebo and promising efficacy.8,9

Objectives

• To evaluate changes in hematuria grade and serum Gd-IgA1 quartiles over 36 weeks with atacicept 150 mg vs placebo

• To evaluate the association between changes in Gd-IgA1 and hematuria grade at week 36

Methods

• Microscopic hematuria
  - Evaluated on urine dipstick; participants with hematuria 1+ or higher at baseline were evaluated for improvement at week 36

• Serum Gd-IgA1
  - Assessed at baseline, 4, 12, 24, and 36 weeks using a solid phase sandwich enzyme immunoassay kit (ELISA Kit) (Immuno-Biological Laboratories, Inc., Minohmachi, Mino; by a central laboratory at Medpace (Cincinnati, OH) and classified into quartile studies using cutoffs derived from baseline Gd-IgA1 values from the ORIGIN population

• Relationship between Gd-IgA1 % change from baseline and hematuria grade at week 36
  - Evaluated using Spearman's correlation method

Results

Hematuria Improvement and Lower Gd-IgA1 Quartiles at Week 36

- In the placebo group, all 9 participants with the highest baseline Gd-IgA1 quartile, 4, remained in quartile 3 or 4 at the last nonmissing visits

- In the atacicept 150 mg group, all 8 participants with the highest baseline quartile had reductions to quartile 1 or 2 at the last nonmissing visits

Lower Gd-IgA1 Quartiles Through Week 36

- In the atacicept 150 mg group, most participants on placebo transiently increased or decreased by 1 quartile

Conclusions

• In addition to clinically and statistically significant effects on renal function, atacicept 150 mg achieved an improvement in hematuria and a durable and significant Gd-IgA1 reduction over 36 weeks

• Hematuria improved to negative or trace in most participants receiving atacicept 150 mg (80% vs 5% placebo)

• Regardless of baseline serum Gd-IgA1 quartile, the vast majority of participants receiving atacicept 150 mg for 36 weeks achieved Gd-IgA1 reductions to the lowest quartiles, which has been associated with improved renal clinical outcomes

• Greater Gd-IgA1 reduction was associated with lower grades of hematuria at week 36

• These results provide further evidence supporting atacicept as a potential disease-modifying treatment for IgAN

References:


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