Abstract Type : Oral presentation
Abstract Submission No.: A-0339
Abstract Topic : Glomerular and Tubulointerstitial Disorders

Longer Follow-Up of Povetacicept Shows Potential for Treatment of Primary Membranous Nephropathy (RUBY-3 Study)

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Objectives : pMN is caused by pathogenic B-cells that produce autoantibodies, such as anti-PLA2R, which attach to autoantigens on podocytes, resulting in glomerular injury. BAFF and APRIL are central to pMN pathogenesis by promoting survival and maturation of pathogenic transitional and naïve B-cells, T-cell-independent B-cell responses to certain antigens, B-cell regulation, and Ig class-switch recombination. Povetacicept, a dual inhibitor of BAFF and APRIL, represents a significant therapeutic advancement by targeting the root cause of disease. Updated interim data for participants dosed with povetacicept in the RUBY-3 study are provided.
Methods : RUBY-3 is an ongoing Phase 1/2, open-label study in adults with pMN, receiving povetacicept 80 mg subcutaneously administered Q4W (n=10 dosed; n=5 at 24 weeks). Primary objective: evaluation of the safety of povetacicept. Secondary objectives: efficacy, PK, and biomarker changes with povetacicept treatment.
Results : Data at 24 weeks (n=5) indicate mean 24-hour UPCR decreased 57% (from 3.8 g/g to 1.6 g/g) and eGFR was stable. By Week 24, 80% (4/5) of participants achieved immunologic remission, 60% (3/5) of participants achieved partial clinical remission, and mean anti-PLA2R autoantibody declined from baseline by 78%. In the subset of 3 participants at moderate to high risk of disease progression defined by baseline 24-hour UPCR >3.5 g/g, at Week 24, mean 24 hour UPCR decreased by 62% (from 5.0 g/g to 1.9 g/g); eGFR was stable; 67% (2/3) participants achieved immunologic remission and partial clinical remission; and anti-PLA2R autoantibodies declined 90%. Povetacicept was generally safe and well tolerated.

Conclusions : Povetacicept was generally safe and well tolerated in adults with pMN through 24 weeks and resulted in substantial reductions in UPCR and anti-PLA2R autoantibody and stable eGFR including in subjects at high risk of disease progression. These updated data reinforce the potential of povetacicept as therapy for pMN.

RUBY-3 Study, Anti-PLA2R Autoantibody Mean Percentage Change from Baseline to Week 24.jpg