Zanubrutinib (zanu) in anti-phospholipase A2 receptor (PLA2R)-associated primary membranous nephropathy (PMN): Preliminary results of a Phase 2/3, multicenter, randomized, open-label study

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ABSTRACT

Background: BTK plays a role in B-cell modulation and is a potential target in PMN. Zanu (BTK inhibitor) is being evaluated in a 2-part study in PMN (NCT05707377). Part 1 data are shown.

Methods: After a 12-wk run-in, pts with PLA2R antibody >50 RU/mL and urinary protein-creatinine ratio (UPCR) >3.5 g/g received zanu 160 mg twice daily for 64 wks, followed by 40-wk observation. The efficacy endpoints include change from baseline in anti-PLA2R antibody titer, UPCR, clinical remission rate and safety.

Results: As of March 7, 2025, 30 pts were treated; median age: 46.5 (range 32-74) yrs, 66.7% male, 90.0% were from Asia. At baseline, mean UPCR was 7.8 mg/mg (SD 3.0), median serum anti-PLA2R antibody was 161.0 RU/mL (range 51.4-1219.8), mean serum albumin was 25.4 g/L (SD 7.2), median eGFR was 85.2 mL/min/1.73m^2 (range 39.8-123.0). Median exposure: 57 wks. At 52 wks, mean UPCR change from baseline: -4.9 mg/mg (SD 2.5), a 70.4% reduction overall (**Fig 1**). 5 pts had complete remission (UPCR ≤0.3 mg/mg and stable eGFR) and 8 pts had partial remission (UPCR of >0.3 to ≤3.5 mg/mg, with ≥50% decrease from baseline, and stable eGFR), resulting in a total remission rate of 43.3%. **Fig 2:** change in PLA2R antibody. Immunological response rate (anti-PLA2R titer reduction to <14 RU/mL) was 56.7%. 27 pts (90.0%) had treatment-emergent adverse events (TEAEs); most common: upper respiratory tract infection (30.0%), rash, anemia (both 23.3%). Four pts (13.3%) had severe TEAEs (two treatment-related).

Conclusion: Zanu is generally well tolerated with promising efficacy in pts with primary PMN; continued evaluation in pts with PMN is supported.

Figures

Figure 1. Mean change in UPCR from baseline at each study visit

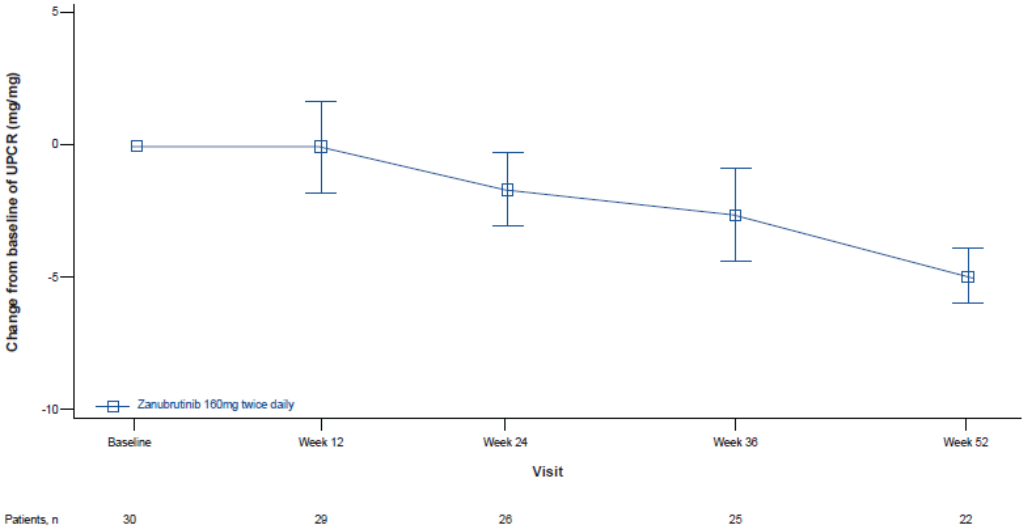

Figure 2. Median change in serum anti-PLA2R antibody from baseline at each study visit