Zanubrutinib for the treatment of primary membranous nephropathy (PMN): Results of a single-arm feasibility study

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ABSTRACT

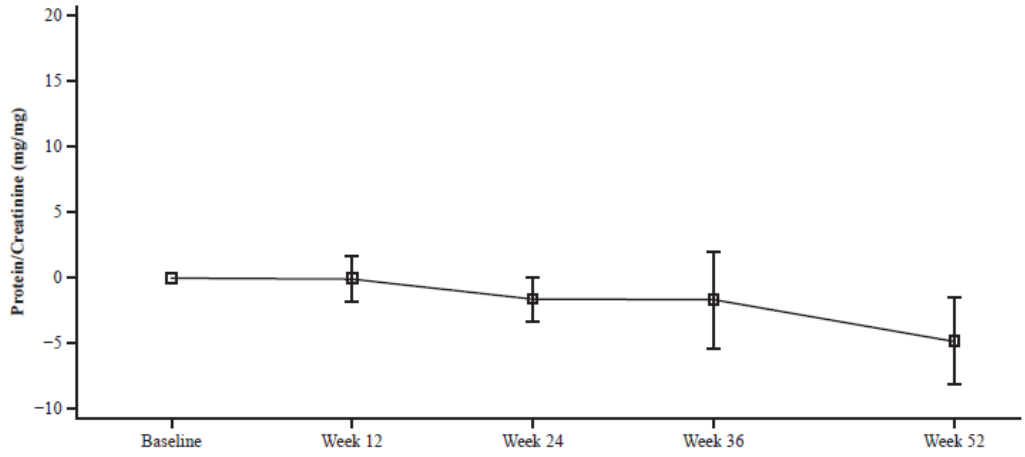
Background: Bruton tyrosine kinase (BTK) plays a key role in B cell modulation and is a potential therapeutic target in PMN, an antibody-driven glomerular disease. The efficacy and safety of zanubrutinib, a highly selective inhibitor of BTK, is being evaluated in a 2-part, phase 2/3 open-label study in patients (pts) with PMN. Here, part 1 is presented.

Methods: After a 12-wk run-in with optimal supportive care, pts with anti-phospholipase A2 receptor (PLA2R) antibody (Ab) >50 RU/mL and urinary protein-creatinine ratio (UPCR) >3.5 g/g receive zanubrutinib 160 mg BID for 64 wks, followed by a 40-wk observation period. Primary endpoint: change from baseline in UPCR at wk 24; secondary endpoints: anti-PLA2R Ab titer, serum albumin, overall remission rate, safety.

Results: Of 30 pts, most were men (66.7%) and Asian (93.3%). At baseline, median (range) UPCR was 7.5 g/g (3.6, 14.8), serum anti-PLA2R Ab was 161.0 (51.4, 1219.8) RU/mL, serum albumin was 23.5 (15.4, 42.3) g/L, and eGFR was 85.2 (39.8, 123.0) mL/min/1.73m^2. As of July 15, 2024, the median duration of exposure was 26.5 wks, and 20 pts had completed the wk 24 visit (5 pts discontinued early). At 24 wks, median change from baseline in UPCR was -1.5 g/g (-8.8, 5.7); 6 pts (30%) had partial remission (UPCR 0.3–3.5 g/g and ≥50% decrease from baseline, stable eGFR), and the immunological response rate (anti-PLA2R titer reduction to <14 RU/mL) was 60% (**Figure**). Overall, 26 pts (87%) had treatment-emergent adverse events (TEAEs), mostly (≥15% pts) upper respiratory tract infections (27%), rash (20%), and hypokalemia (17%). 4 pts (13%) had severe TEAEs (treatment-related in 1 pt).

Conclusions: Zanubrutinib appears to be generally well tolerated and shows activity in pts with PMN.

A



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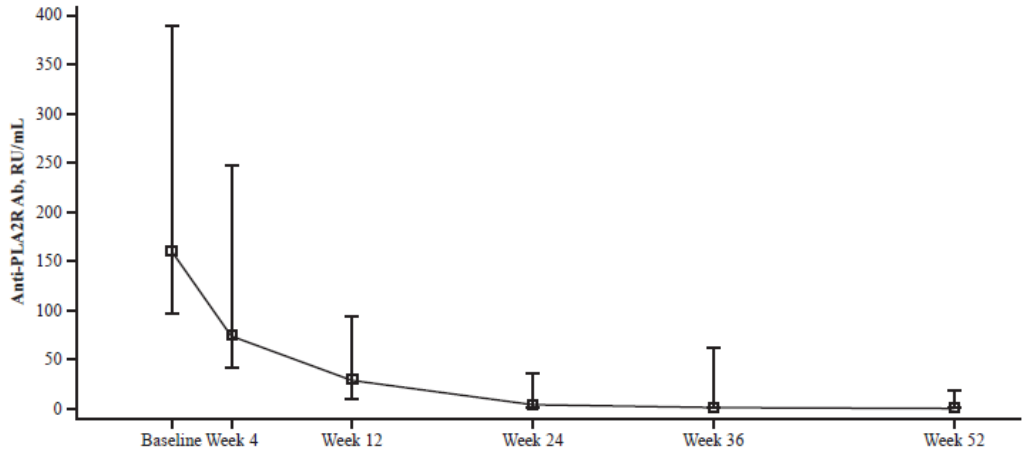

Patients by analysis visit, n

UPCR	30		29	20	8	3
Anti-PLA2R Ab	30	30	28	20	5	3

Beneficial changes observed in (**A**) mean (95% CI) UPCR change from baseline and (**B**) median (IQR) serum anti-PLA2R Ab titer over time