A Phase 2/3, Multicenter, Randomized, Active-Controlled, Open-Label Study to Evaluate the Efficacy and Safety of Zanubrutinib in Patients With Primary Membranous Nephropathy

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Background

Primary membranous nephropathy (pMN) occurs when B cells produce pathogenic autoantibodies against M-PLA2R on podocytes. There are no approved therapies for pMN. Bruton tyrosine kinase (BTK) plays a pivotal role in B-cell receptor signaling; inhibition of BTK may be a promising therapeutic target for pMN. Zanubrutinib is a next-generation BTK inhibitor aimed to maximize BTK occupancy and minimize off-target effects. Here we introduce a study to evaluate the safety and efficacy of zanubrutinib in patients (pts) with pMN.

Methods

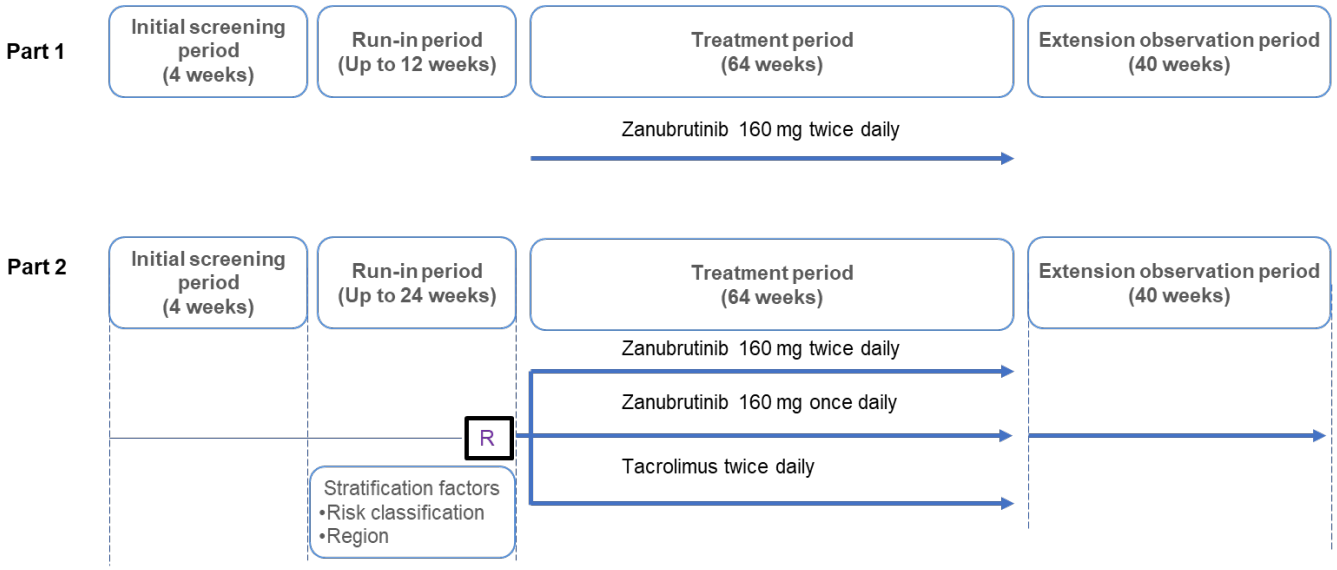
ALMOND (BGB-3111-309; NCT05707377) is a 2-part, phase 2/3, multicenter study investigating zanubrutinib in adults aged 18-75 y with biopsy-confirmed pMN. Eligible pts must have a urine protein:creatinine ratio (UPCR) >3.5 (based on 24-h collection) and treatment with a maximally tolerated dose of an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker for ≥24 wk (12 wk in part 1) with adequate blood pressure control before the assignment of study treatment, and anti-PLA2R antibodies >50 RU/mL at screening confirmation assessment (part 1 only).

Part 1 (open-label, single-arm design) will evaluate the efficacy and safety of zanubrutinib 160 mg BID for 64 wk in 30 pts. Part 2 (randomized, open-label, 3-arm with active-control design) will evaluate zanubrutinib 160 mg BID, zanubrutinib 160 mg QD, or tacrolimus 0.05 mg/kg/d for 64 wk in 252 pts (n=84 in each arm). The primary outcomes are reduction in UPCR (part 1) and the number of pts achieving complete remission (part 2). Secondary outcomes include safety and pts with treatment failure, immunological response, complete or partial remission, and relapse. Secondary outcomes specific to art 2 include time to first complete remission or partial remission, time to first relapse, pts with ≥30% eGFR reduction, and health-related quality of life assessments.

Conclusion

Study enrollment is ongoing.

Figure 1. Study Schema



R, randomization.