TPS7088 **Poster Session**

Efficacy and safety of nemtabrutinib in relapsed or refractory chronic lymphocytic leukemia/small lymphocytic lymphoma: Cohort J of the phase 2 BELLWAVE-003 study.

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Background: Treatment options for patients with relapsed or refractory (R/R) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) can be limited if patients do not respond to both Bruton tyrosine kinase inhibitors (BTKis) and B-cell lymphoma 2 inhibitors (BCL2is). Nemtabrutinib is a once-daily, potent, noncovalent, reversible BTKi with a distinct kinase profile that inhibits BTK and other B-cell receptor relevant kinases. The multicenter, open-label, single-arm, phase 2 BELLWAVE-003 study (NCT04728893) is designed to evaluate nemtabrutinib at the recommended phase 2 dose (RP2D) in participants with R/R CLL/SLL, Richter transformation, mantle cell lymphoma, marginal zone lymphoma, follicular lymphoma, and Waldenström macroglobulinemia. Cohort J will evaluate nemtabrutinib in participants with R/R CLL/SLL who are relapsed/refractory to both a BTKi and BCL2i. **Methods:** Key eligibility criteria for cohort J include participants aged ≥18 years with CLL/SLL whose disease is R/R to prior therapy with both a BTKi (covalent or irreversible) and a BCL2i, and an ECOG PS of 0 to 2. Additional use of noncovalent or reversible BTKis is permitted if disease is R/R to such therapy. Participants must have received and not responded to, been intolerant to, or determined by their treating physician to be a poor PI3Ki candidate or ineligible for PI3Ki per local (institution) guidelines. Exclusion criteria include prior exposure to nemtabrutinib, active CNS disease, and prior systemic therapy with a monoclonal antibody within 5 half-lives or 4 weeks before allocation. Overall, the BELLWAVE-003 study comprises a dose escalation and confirmation phase (part 1) to establish the RP2D, and a cohort expansion phase (part 2). Part 1 evaluated nemtabrutinib in ≥6 to ≤20 participants with R/R CLL/SLL after ≥2 prior lines of therapy. The RP2D has been established as nemtabrutinib 65 mg QD. In part 2, ~460 participants will be enrolled across 9 expansion cohorts. Approximately 40 participants will be enrolled in cohort J. Treatment will continue until unacceptable toxicity, disease progression, or withdrawal. Adverse events will be monitored throughout and graded using NCI CTCAE version 5.0. Hematologic toxicities in participants with CLL will be assessed using iwCLL 2018 criteria. CT/MRI and/or PET will be performed every 12 weeks unless needed more frequently. The primary end point for cohort J is ORR per iwCLL 2018 criteria by independent central review (ICR). Additional end points include DOR and PFS per iwCLL 2018 criteria by ICR, OS, and safety and tolerability. Recruitment is ongoing. This is the first clinical trial with a dedicated cohort to assess noncovalent BTKis in patients whose disease has failed to respond to both BTKi and BCL2i. Clinical trial information: NCT04728893. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.