TPS6587 **Poster Session**

Shorespan-007: Phase 3 study of bomedemstat versus hydroxyurea in essential thrombocythemia naive to cytoreductive therapy.

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Background: Lysine-specific demethylase 1 (LSD1) is an enzyme that regulates hematopoietic stem and progenitor cell proliferation and maturation. Bomedemstat (MK-3543) is an LSD1 inhibitor shown to have manageable safety and improve symptoms, durably reduce platelet and white blood cell (WBC) count, and reduce mutation burden in patients with essential thrombocythemia (ET) in a phase 2 study. Here, we describe the methodology of the randomized, double-blind, phase 3 Shorespan-007 study (NCT06456346), which has been designed to evaluate the efficacy and safety of bomedemstat compared with hydroxyurea in participants with ET naive to cytoreductive therapy. **Methods:** Key eligibility criteria include patients aged ≥18 years with an ET diagnosis per WHO diagnostic criteria for myeloproliferative neoplasms, an indication for cytoreductive therapy, no prior cytoreductive therapy, a bone marrow fibrosis score of 0 or 1, a platelet count of $>450 \times 10^9$/L, and an absolute neutrophil count of $\geq 0.75 \times 10^9$/L. Key exclusion criteria include a documented increased risk of bleeding or an active infection necessitating systemic therapy. Approximately 300 participants will be enrolled. Participants will be randomly assigned 1:1 to bomedemstat at a starting dose of 50 mg/day by mouth titrated to a target platelet count of $\geq 150 \times 10^9$/L to $\leq 350 \times 10^9$/L or hydroxyurea at a starting dose of 500 mg/day by mouth titrated per the approved product labeling. The primary end point is durable clinicohematologic response, defined as the following: a confirmed reduction of platelet count to $\leq 400 \times 10^9$/L; absence of a WBC count elevation to $>10 \times 10^9$/L locally assessed to be due to ET; and, if WBC count is elevated to $>10 \times 10^9$/L at screening, a reduction of WBC count to $\leq 10 \times 10^9$/L (confirmed by first subsequent visit a minimum of 2 weeks apart, starting by week 24 and maintained for ≥24 weeks to at least week 48; absence of any thrombotic or major hemorrhagic events or disease progression to myelofibrosis [MF] or myelodysplastic syndrome [MDS]/acute myeloid leukemia (AML) by week 52). Secondary end points include change in fatigue from baseline per the MFSAF v4.0, change in total fatigue score from baseline per the PROMIS Fatigue SF-7a scale, change in total symptom score from baseline per the MFSAF v4.0, duration of clinicohematologic response, duration of hematologic remission, incidence of thrombotic events, incidence of major hemorrhagic events, transformation to post-ET MF or MDS/AML, and safety and tolerability. Clinic visits will occur every 2 weeks for the first 12 weeks and every 4 weeks thereafter. Adverse events will be monitored throughout the study and for ≤30 days after treatment end and will be graded per NCI CTCAE v5.0. Recruitment for Shorespan-007 is ongoing or planned in sites in Asia, Australia, Europe, North America, and South America. Clinical trial information: NCT06456346. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.