TPS6588 Poster Session

IMpactMF, randomized, open-label, phase 3 trial of imetelstat (IME) versus best available therapy (BAT) in patients (pts) with intermediate-2 (INT-2) or high-risk (HR) myelofibrosis (MF) relapsed or refractory (R/R) to Janus kinase inhibitors (JAKi).

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Background: IME is a first-in-class telomerase inhibitor approved in 2024 for pts with transfusion-dependent lower-risk myelodysplastic syndromes who are R/R or ineligible for erythropoiesis-stimulating agents. In the phase 2 IMbark trial (NCT02426086) in pts with MF, IME (9.4 mg/kg every 3 weeks [q3w]; N=59) at wk 24 showed median overall survival (OS) of 29.9 mo (median follow-up, 27.4 mo), total symptom score reduction ≥50% in 32% of pts, and spleen volume reduction ≥35% in 10% of pts. IME treatment dose-dependently improved bone marrow (BM) fibrosis and reduced MF driver mutation variant allele frequency, which correlated with improved OS. The most common grade ≥3 adverse events were thrombocytopenia, anemia, and neutropenia; cytopenias were generally manageable, short-lived, and resolved to grade ≤2 in <4 wks. These data support further evaluation of IME. **Methods:** IMpactMF (MYF3001; NCT04576156) is a phase 3, open-label, randomized (2:1) trial of IME versus BAT in ≈320 adults with INT-2 or HR MF R/R to JAKi or ineligible for allogeneic stem cell transplantation or further JAKi. Randomization is to IME sodium 9.4 mg/kg (8.9 mg/kg active dose) intravenously q3w or investigator-selected BAT (eg, hypomethylating agents, hydroxyurea, interferon, thalidomide, danazol, chemotherapy, or other non–JAKi-containing therapy, but not hematopoietic stem cell transplantation or splenectomy). Eligibility criteria include peripheral blood and marrow blast counts <10% and Eastern Cooperative Oncology Group performance status ≤2. Chronic liver disease unrelated to underlying MF, active systemic hepatitis infection, or clinically significant cardiovascular disease are not allowed. Pts are stratified at randomization based on INT-2 or HR MF per the Dynamic International Prognostic Scoring System and baseline platelet count. Crossover to IME may be permitted for pts who meet progressive disease criteria (≥25% increase in spleen volume from baseline) or a palpable increase in splenomegaly after 6 mo of BAT. IMpactMF is the first MF phase 3 trial evaluating OS as the primary endpoint. Secondary endpoints include wk 24 symptom and spleen response rates, progression-free survival, clinical response assessments per modified 2013 International Working Group-Myeloproliferative Neoplasms Research and Treatment criteria, time to and duration of response, reduction in BM fibrosis, safety, pharmacokinetics, and pt-reported outcomes. Biomarkers and mutation analyses will be performed. As of December 2024, 172 sites in North and South America, Europe, Middle East, Australia, and Asia have enrolled ≈75% of pts. The planned interim analysis (when ≈35% of pts planned to be enrolled have died) is expected in early 2026 and final analysis is expected in early 2027. Clinical trial information: NCT04576156. Research Sponsor: This study was funded by the Geron Corporation; writing and editorial support were provided by Meredith Rogers, MS, CMPP, of The Lockwood Group (Stamford, CT, USA), funded by the Geron Corporation.