TPS6583 **Poster Session**

A phase II open-label study of olutasidenib post-transplant maintenance therapy for patients with IDH1-mutated myeloid malignancies.

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Background: Allogeneic hematopoietic stem cell transplantation (alloSCT) remains one of the most effective treatments for patients with myeloid malignancies. Much of the benefit is due to the immune-mediated graft-versus-leukemia effect to prevent relapse. Nevertheless, despite advances in conditioning therapy, disease relapse remains the most important cause of treatment failure after alloSCT. Maintenance therapy post alloSCT aims to reduce relapse incidence and strengthen the potential for cure. With modern treatment regimens, expected complete remission (CR) rates for newly diagnosed AML patients are 60-70%, however, long-term cure rates are only ~30% and improved treatments are needed. IDH1 mutations occur in >7% of older patients with AML and up to 4% of patients with high-risk CMML or MDS. A multicenter phase I trial of another IDH1 inhibitor used as maintenance treatment following alloSCT for IDH1-mutated AML demonstrated a two-year progression-free survival (PFS) of 81%, and two-year overall survival (OS) of 88%. The 2-year cumulative incidence of disease relapse was 19% (95% CI, 4%–41%) and the 2-year cumulative incidence of non-relapse mortality (NRM) was 0%. Olutasidenib is a well-tolerated, highly selective, non-cytotoxic, and potent FDA-approved oral inhibitor of mutant IDH1, with an overall response rate in relapsed/refractory AML of 48%. **Methods:** In our single center, investigator-initiated study under the MDACC-Rigel Research Alliance we aim to determine the safety and tolerability of olutasidenib as maintenance post-allo-SCT and to determine the rate of progression-free survival (PFS). Eligibility includes patients 18-75 years old with IDH1 mutation presence at diagnosis with acceptable organ function. Patients must also have a diagnosis of AML, MDS, MPN, or CMML according to World Health Organization (WHO) classification that underwent first or second alloSCT with either peripheral blood or bone marrow hematopoietic stem cell source, regardless of donor type/match, conditioning regimen, or GVHD prophylaxis and is at least 30 days post stem cell transplant until day 120. A safety lead-in phase will be given for the first 6 patients to investigate whether the starting dose of 150 mg BID is safe and tolerable. After the safety lead-in phase, the remaining patients will be enrolled at the same dose and the safety and tolerability will be monitored. We also would like to determine response rate, overall survival (OS), cumulative incidence of relapse, NRM, GVHD relapse-free survival (GRFS), rate and grading of aGVHD grade 2-4 and 3-4 at day 100, incidence and grading chronic GVHD (cGVHD) all grades. The goal enrollment is 25 total patients. The study was activated and enrollment began in December 2024. Clinical trial information: NCT06668584. Research Sponsor: None.