

Magrolimab In Combination With Azacitidine for Patients With Untreated Higher-Risk Myelodysplastic Syndromes (HR MDS): 5F9005 Phase 1b Study Results

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Context: Magrolimab is a monoclonal antibody blocking CD47, a “don’t eat me” signal overexpressed on cancer cells, which leads to tumor phagocytosis and is synergistic with azacitidine. A high unmet need exists to build on current standard-of-care azacitidine in patients with HR MDS. Objective: Report final safety/tolerability and efficacy data. Design: Phase 1b trial of magrolimab+azacitidine (NCT03248479). Patients: 95 patients with untreated HR MDS (intermediate, high, or very-high risk per the Revised International Prognostic Scoring System [IPSS-R]). Interventions: Magrolimab IV 1-mg/kg (priming) then 30-mg/kg ramp-up QW/Q2W (maintenance). Azacitidine 75 mg/m² IV/SC days 1-7 (each 28-day cycle). Main Outcome Measures: Primary endpoints were safety/ tolerability and complete remission (CR) rate. Results: Median age was 69y [range, 28-91y]. IPSS-R risk was intermediate, high, or very high in 27%, 52%, and 21% of patients, respectively. Therapy-related MDS, TP53 mutation, and poor-risk cytogenetics were reported in 22%, 26%, and 62% of patients, respectively. Median number of cycles was 6 (range, 1-27). The most common treatment-emergent adverse events (TEAEs) included constipation (68%), thrombocytopenia (55%), anemia (52%), neutropenia (47%), nausea (46%), and diarrhea (43%). The most common grade 3/4 TEAEs included anemia (47%), neutropenia (46%), thrombocytopenia (46%), and white blood cell count decreased (30%). Six patients discontinued treatment due to AEs. The 60-day mortality rate was 2%. Median hemoglobin change from baseline at first post dose sample was -0.7 g/dL (range, -3.1 to 2.4 g/dL). CR and objective response (OR) rates were 33% and 75%; 31% of OR-evaluable patients with baseline abnormal cytogenetics had cytogenetic CR. Median time to first OR, duration of CR, duration of OR, and progression-free survival were 1.9, 11.1, 9.8, and 11.6 months, respectively. 12- and 24-month overall survival (OS) rates were 75% and 52%, respectively; median OS was not reached with 17.1 months of follow-up. Favorable outcomes were

observed in patients with TP53 mutation (n=25; CR rate, 40%; median OS, 16.3 months) and wild-type TP53 (n=61; CR rate, 31%; median OS, not reached). Conclusions: Magrolimab+azacitidine was well tolerated, with promising efficacy in patients with untreated HR MDS, including those with TP53-mutated and –wild-type disease. A Ph3 trial of magrolimab/placebo+azacitidine (ENHANCE; NCT04313881) is ongoing. Keywords: MDS, myelodysplastic syndromes, magrolimab, azacitidine, CD47, TP53, Phase I