

Tolerability and Efficacy of the First-In-Class Anti-CD47 Antibody Magrolimab Combined With Azacitidine in Frontline Patients With TP53-Mutated Acute Myeloid Leukemia (AML): Phase 1b Results

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Context: Patients with TP53-mutated AML have a poor prognosis. Magrolimab is an antibody blocking CD47, a “don’t eat me” signal on cancer cells, which induces tumor phagocytosis and is synergistic with azacitidine. Objective: Report final tolerability and efficacy data.

Design: Ph1b single-arm trial of magrolimab+azacitidine (NCT03248479). Patients: 72 frontline patients with TP53-mutated AML unsuitable for intensive chemotherapy. 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: Common treatment-emergent adverse events (TEAEs) were constipation (52.8%), diarrhea (47.2%), febrile neutropenia (45.8%), nausea (43.1%), fatigue (37.5%), decreased appetite (37.5%), thrombocytopenia (31.9%), peripheral edema (30.6%), and cough (30.6%). Common grade (G) ≥3 TEAEs were febrile neutropenia (37.5%), anemia (29.2%; G3, 26.4%; G4, 2.8%), thrombocytopenia (29.2%), pneumonia (26.4%), and neutropenia (20.8%). G3 hemolysis was reported in 1 patient; no G4 hemolysis was reported. Objective response rate was 48.6% (CR, 33.3%; CR with incomplete hematologic recovery [CRi]/CR with partial hematologic recovery [CRh], 8.3%; morphologic leukemia-free state [MLFS], 1.4%; partial remission, 5.6%). 16.7% and 5.6% of patients had stable disease and progressive disease (PD), respectively; 30- and 60-day mortality rates were 8.3% and 18.1%, respectively. Response assessments were unavailable in 4.2% discontinued due to AEs) and 6.9% (other) of patients prior to the C3D1 assessment. Median time to CR/CRi was 2.2 months (range, 1.7-7.2) and CR was 3.0 months (range, 1.8-9.6); 14/31 (45.2%) evaluable patients with CR/CRi/CRh/MLFS achieved negative MRD. 8/24 patients with CR had a longitudinal TP53 variant-allele-frequency (VAF) assessment; 5/8 (63%) had ≥5% VAF. Treatment was stopped due to stem cell transplant (9 [12.5%]), PD (26 [36.1%]), death (8 [11.1%]), AE (13 [18.1%]),

or other (14 [19.4%]). Median durations of CR and CR/CRi were 7.7 (95% CI, 4.7-10.9) and 8.7 (95% CI, 5.3-10.9) months, respectively. Median overall survival was 10.8 months (95% CI, 6.8-12.8; 8.3-month median follow-up). Conclusions: Magrolimab+azacitidine showed durable responses and encouraging overall survival in frontline patients with TP53-mutated AML unsuitable for intensive chemotherapy. A Ph3 trial of magrolimab+azacitidine vs standard- of-care in TP53-mutated AML (ENHANCE-2; NCT04778397) is ongoing. Keywords: AML, acute myeloid leukemia, magrolimab, azacitidine, CD47, TP53, Phase I.