

AML-399

A Phase 2, Open-Label, Multiarm, Multicenter Study to Evaluate Magrolimab Combined With Antileukemia Therapies for First-Line, Relapsed/Refractory, or Maintenance Treatment of Acute Myeloid Leukemia (AML)

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Context: Patients with newly diagnosed AML who are ineligible for intensive chemotherapy (IC) are incurable, despite progress with azacitidine + venetoclax, whereas patients with relapsed/refractory disease continue to have a poor prognosis. Furthermore, relapse remains frequent for patients in remission receiving oral azacitidine. Magrolimab is a blocking antibody against CD47, a “don’t eat me” signal overexpressed on cancer cells. This blockade induces tumor phagocytosis and is synergistic with chemotherapy and hypomethylating agents. Magrolimab + azacitidine has demonstrated encouraging efficacy in newly diagnosed AML (objective response rate [ORR], 63%; complete remission [CR], 42%).

Objective: To evaluate the safety/tolerability and efficacy of magrolimab combined with antileukemia therapies in patients with newly diagnosed or relapsed/refractory AML or with AML in maintenance post-IC. **Design:** This open-label, multi-arm, multicenter study includes 3 safety run-ins with corresponding expansion cohorts (NCT04778410). Safety run-in cohorts will enroll 6 patients for 28 days to determine dose-limiting toxicities and the recommended phase 2 dose prior to enrollment of phase 2 cohorts. **Patients:** Patients must be aged ≥75 or 18–74 years with comorbidities precluding IC (cohort [C]1), have relapsed/primary refractory disease post-IC (C2), or have CR/CR with incomplete hematologic recovery and measurable residual disease (MRD) post-IC (C3). **Interventions:** Patients will receive magrolimab + venetoclax + azacitidine (C1), magrolimab + mitoxantrone + etoposide + cytarabine (MEC; C2), or magrolimab + CC-486 (C3). In all cohorts, magrolimab will be administered intravenously with priming and ramp-up doses of 1 (day [D]1, D4), 15 (D8), and 30 mg/kg (D11, D15, then QW [×5], followed by Q2W). Azacitidine, venetoclax, MEC, and CC-486 will be administered per label indications. After completion of the safety run-ins, additional patients will be enrolled into the phase 2 study (C1, n=40; C2, n=30; C3, n=40). Study treatments will follow the dosing schedule until disease progression, unacceptable toxicity, or loss of clinical benefit (C1/C3) or for 2 to 3 cycles for MEC with a maximum 12 months of magrolimab (C2). **Main Outcome Measures:** Primary efficacy endpoints are CR rate (C1/C2) and MRD-negative CR rate (C3). Secondary endpoints include overall survival, ORR, and MRD negativity (C1/C2).

Keywords: AML, acute myeloid leukemia, magrolimab, azacitidine, venetoclax, CD47, Trial-in-Progress