# THE FIRST-IN-CLASS ANTI-CD47 ANTIBODY MAGROLIMAB COMBINED WITH AZACITIDINE IS WELL-TOLERATED AND EFFECTIVE IN AML PATIENTS: PHASE 1B RESULTS

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## Background

Magrolimab (Hu5F9-G4) is an antibody blocking CD47, a macrophage immune checkpoint and don't eat me signal on cancers. It induces tumor phagocytosis and eliminates leukemia stem cells. Azacitidine (AZA) synergizes with magrolimab by inducing eat me signals on leukemic blasts, enhancing phagocytosis. We report here Ph1b data in untreated AML, including *TP53* mutant patients.

## Aims

This Ph1b study aimed to determine the safety and efficacy of magrolimab + AZA in untreated AML patients unfit for intensive chemotherapy.

## Methods

Magrolimab+AZA was given to untreated AML patients who were unfit for intensive chemotherapy. Based on initial encouraging data and high unmet medical need, this cohort was amended to preferentially enroll *TP53* mutant patients. A magrolimab priming/intrapatient dose escalation regimen (1-30 mg/kg QW, Q2W Cycle 3+) was used. AZA was dosed 75mg/m$^2$ on days 1-7. Efficacy was assessed by ELN 2017 criteria.

## Results

29 AML patients with a median age of 74 years (range 60 – 89) were treated with magrolimab + AZA. 7% were intermediate cytogenetic risk and 72% poor risk (21% unknown/missing). 66% had AML with myelodysplasia-related changes, 10% therapy-related AML and 45% were *TP53* mutant. The combo was well tolerated with safety similar to AZA alone. Common treatment-related AEs were anemia (31%), neutropenia (28%), fatigue (24%), thrombocytopenia (17%), and nausea (17%). Treatment-related febrile neutropenia was observed in only 1 patient (3%). Only 1 patient (3%) discontinued due to an AE. On target anemia was mostly mild, transient and mitigated by the priming dose regimen with many patients decreasing RBC transfusion requirements on therapy. The mean drop in hemoglobin with the first dose of magrolimab + AZA was only 0.4 g/dL. In RBC transfusion dependent patients, 64% of patients became transfusion independent. In 25 efficacy evaluable patients, 16 (64%) had an objective response (40% CR, 16% CRi, 4% PR, 4% MLFS, 32% SD, 4% PD). Cytogenetic CRs were seen in 50% of evaluable responding patients. 50% of patients with CR/CRi were MRD negative by multiparameter flow cytometry. Median time to response was rapid at 1.9 months, faster than expected with AZA

alone. Median duration of response has not been reached (range 0.03 – 15 mos ongoing), with a median follow-up of 9.4 mos. Median overall survival has also not been reached (range 0.7 – 17.5 mos ongoing).

In 12 untreated TP53 mutant AML patients unfit for induction chemotherapy, the CR/CRi rate was 75% (42% CR, 33% CRi, 17% SD, 8% PD). 50% of patients achieved a cytogenetic CR with 44% achieving MRD negativity in those with CR/CRi. The median duration of response has not been reached (range 0.03 – 15 mos ongoing) with a median follow-up of 8.8 months (range 1.9 – 16.9 mos). 100% of responding patients continue in response at 6 months. The median overall survival has not been reached (range 3.1 – 16.9 mos ongoing) with a 6 mo overall survival estimate of 91%.

## Conclusion

Magrolimab is a novel macrophage targeting immunotherapy that with AZA is well tolerated and effective in AML patients unfit for intensive chemotherapy. Durable efficacy is particularly encouraging in the TP53 mutant AML given the lack of effective therapies in this poor prognostic population. Additional AML patients are enrolling (NCT03248479). Registrational approaches, particularly in TP53 mutant AML, are planned. Additional patients, follow up and translational analyses will be reported at time of presentation. Funded by Forty Seven and the California Institute for Regenerative Medicine.

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