TOLERABILITY AND EFFICACY OF THE FIRST-IN-CLASS ANTI-CD47 ANTIBODY MAGROLIMAB COMBINED WITH AZACITIDINE IN FRONTLINE PATIENTS WITH TP53-MUTATED ACUTE MYELOID LEUKEMIA: PHASE 1B RESULTS

Author(s): Naval G Daver, Paresh Vyas, Suman Kambhampati, Monzr M Al Malki, Richard Larson, Adam Asch, Gabriel Mannis, Wanxing Chai-Ho, Tiffany Tanaka, Terrence Bradley, Deepa Jeyakumar, Eunice Wang, Guan Xing, Mark Chao, Giri Ramsingh, Camille Renard, Indu Lal, Joshua Zeidner, David Sallman

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Background

Patients (pts) with *TP53*-mutated acute myeloid leukemia (AML) have a poor prognosis, with limited responses to currently available therapies and low survival outcomes, representing a significant unmet medical need. Magrolimab is a monoclonal antibody blocking CD47, a “don’t eat me” signal overexpressed on cells in cancers such as AML. This blockade induces phagocytosis of tumor cells and is synergistic with azacitidine (AZA) via upregulation of “eat me” signals.

Aims

To report tolerability and efficacy data from a phase 1b trial of magrolimab + AZA in frontline pts with *TP53*-mutated AML unsuitable for intensive chemotherapy (NCT03248479).

Methods

Frontline pts with AML not suitable for intensive chemotherapy received magrolimab IV starting with a priming dose (1 mg/kg) followed by ramp-up to 30 mg/kg QW or Q2W as the maintenance dose. AZA 75 mg/m^2 was given IV or SC on days 1-7 of each 28-day cycle. Primary endpoints were safety/tolerability and complete remission (CR) rate by European LeukemiaNet (ELN) 2017 criteria.

Results

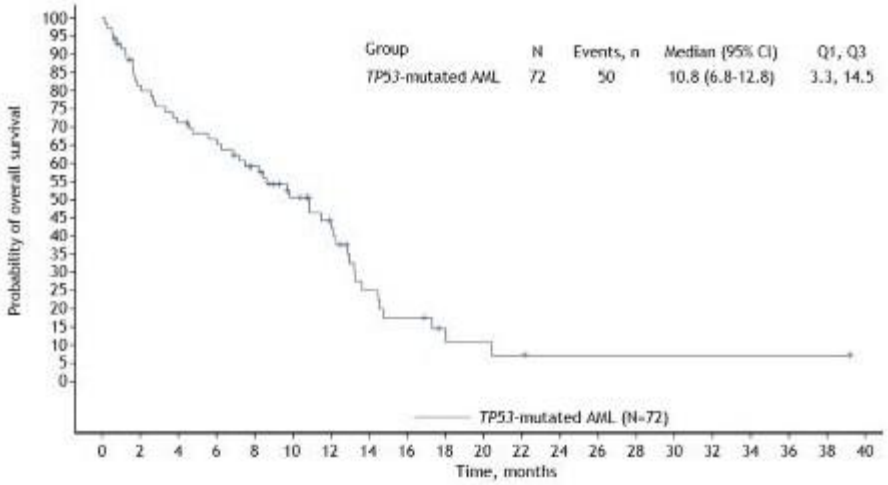
72 pts with *TP53*-mutated AML were treated (Table). Common all-grade treatment-emergent adverse events (TEAEs) were constipation (52.8%), diarrhea (47.2%), febrile neutropenia (45.8%), nausea (43.1%), fatigue (37.5%), decreased appetite (37.5%), thrombocytopenia (31.9%), peripheral edema (30.6%), and cough (30.6%). Most common grade ≥3 TEAEs were febrile neutropenia (37.5%), anemia (29.2%; grade 3, 26.4%; grade 4, 2.8%), thrombocytopenia (29.2%), pneumonia (26.4%), and neutropenia (20.8%). Grade 3 hemolysis was reported in 1 pt (1.4%); no grade 4 hemolysis was reported. Objective response rate by intent to treat 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%). Stable disease and progressive disease (PD) were reported in 16.7% and 5.6% of pts, respectively; 30- and 60-day mortality rates were 8.3% and 18.1%,

respectively. Response assessments were unavailable in an additional 4.2% of pts who discontinued due to AEs and 6.9% due to other reasons, prior to the cycle 3 day 1 assessment. Median time to CR/CRi was 2.2 months (range, 1.7-7.2 months) and to CR was 3.0 months (range, 1.8-9.6 months); 14 of 31 (45.2%) evaluable pts with CR/CRi/CRh/MLFS achieved negative MRD by flow cytometry (investigator reported). Of 24 pts with CR, 8 had a longitudinal *TP53* variant allele frequency (VAF) assessment and 5 of 8 (63%) had VAF decreased to ≤5%. Treatment was stopped due to stem cell transplant (9 [12.5%]), PD (26 [36.1%]), death (8 [11.1%]), AE (13 [18.1%]), and other (14 [19.4%]). Median durations of CR and CR/CRi were 7.7 months (95% CI, 4.7-10.9 months) and 8.7 months (95% CI, 5.3-10.9 months), respectively. Median overall survival (OS) in 72 pts was 10.8 months (95% CI, 6.8-12.8 months) (figure), with median follow-up of 8.3 months.

Table. Baseline characteristics	N=72
Age (range), years	73 (31-89)
ECOG, n (%)	
0-1	61 (84.7)
2	11 (15.3)
ELN cytogenetic risk, n (%)	
Favorable	1 (1.4)
Intermediate	2 (2.8)
Adverse	57 (79.2)
Unknown	12 (16.7)
AML with MDS-related changes, n (%)	34 (47.2)
Therapy-related AML, n (%)	15 (20.8)

ECOG, Eastern Cooperative Oncology Group; MDS, myelodysplastic syndrome.

Figure. OS in frontline pts with *TP53*-mutated AML treated with magrolimab + AZA



Conclusion

In high-risk frontline pts with *TP53*-mutated AML unsuitable for intensive chemotherapy, magrolimab + AZA showed durable responses and encouraging OS in a single-arm study. A Phase 3 trial of this combination vs standard of care in *TP53*-mutated AML (ENHANCE-2; NCT04778397) is ongoing.

Keyword(s): Acute myeloid leukemia, Azacitidine, Immunotherapy, TP53