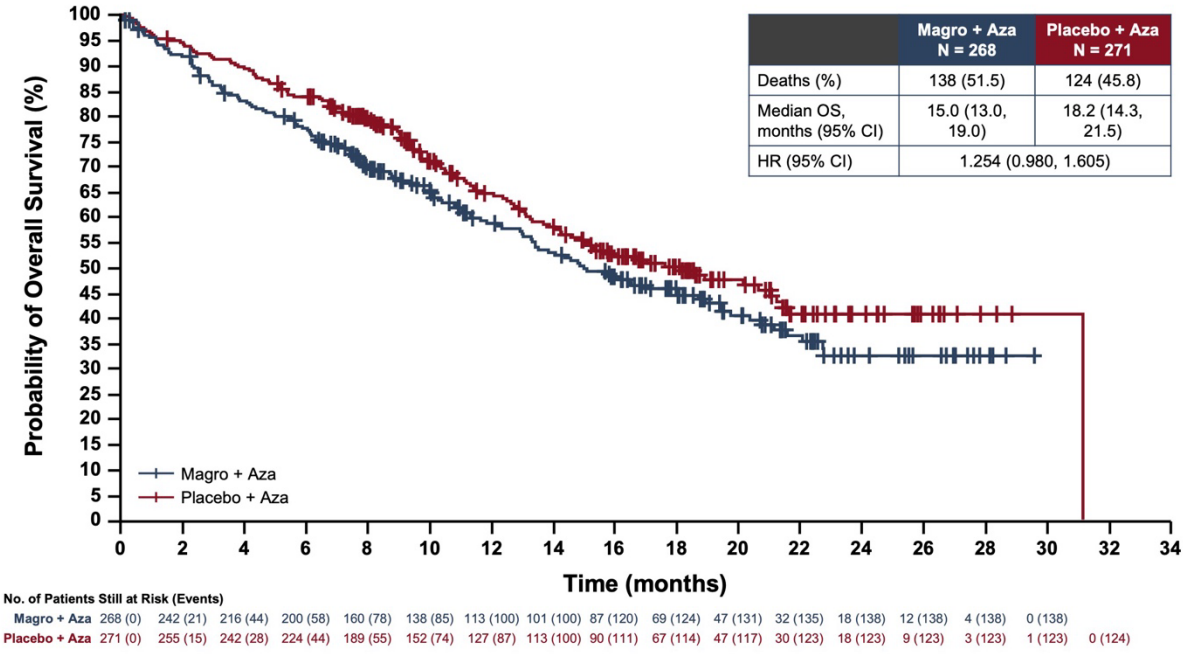
Magrolimab is an investigational agent that has been studied in three separate Phase 3 randomized trials in myeloid disorders including myelodysplastic syndrome and acute myeloid leukemia. The three studies were ENHANCE, ENHANCE-2, and ENHANCE-3. Each of the studies demonstrated that there was a higher risk of death in the magrolimab-containing arm, than the control arm. In the studies where magrolimab was added to standard of care therapy, the incidence of severe, serious, and fatal adverse events was higher in the magrolimab-containing arm. The following are summaries of the ENHANCE, ENHANCE-2, and ENHANCE-3 studies.

ENHANCE

ENHANCE is a phase 3, randomized, double-blinded, controlled trial of azacitidine with and without magrolimab in patients with untreated higher-risk myelodysplastic syndrome. Using a data cutoff date of 19 May 2023, a complete evaluation of safety and efficacy was performed. There were 539 randomized patients included in the analysis. The median follow up was 10.1 months in the magrolimab-containing arm, and 11.1 months in the control arm. For overall survival, there were 138 deaths on the magrolimab-containing arm and 124 deaths on the control arm. 48.5% were censored in the magrolimab-containing arm and 54.2% were censored in the control arm. The hazard ratio of magrolimab-azacitidine arm compared to the control arm was 1.254 (95% CI, 0.980, 1.605), increasing the risk of death by 25% on average compared to the control arm.

Overall Survival: ENHANCE



	Magro + Aza N = 268	Placebo + Aza N = 271
Deaths (%)	138 (51.5)	124 (45.8)
Median OS, months (95% CI)	15.0 (13.0, 19.0)	18.2 (14.3, 21.5)
HR (95% CI)	1.254 (0.980, 1.605)	

No. of Patients Still at Risk (Events)

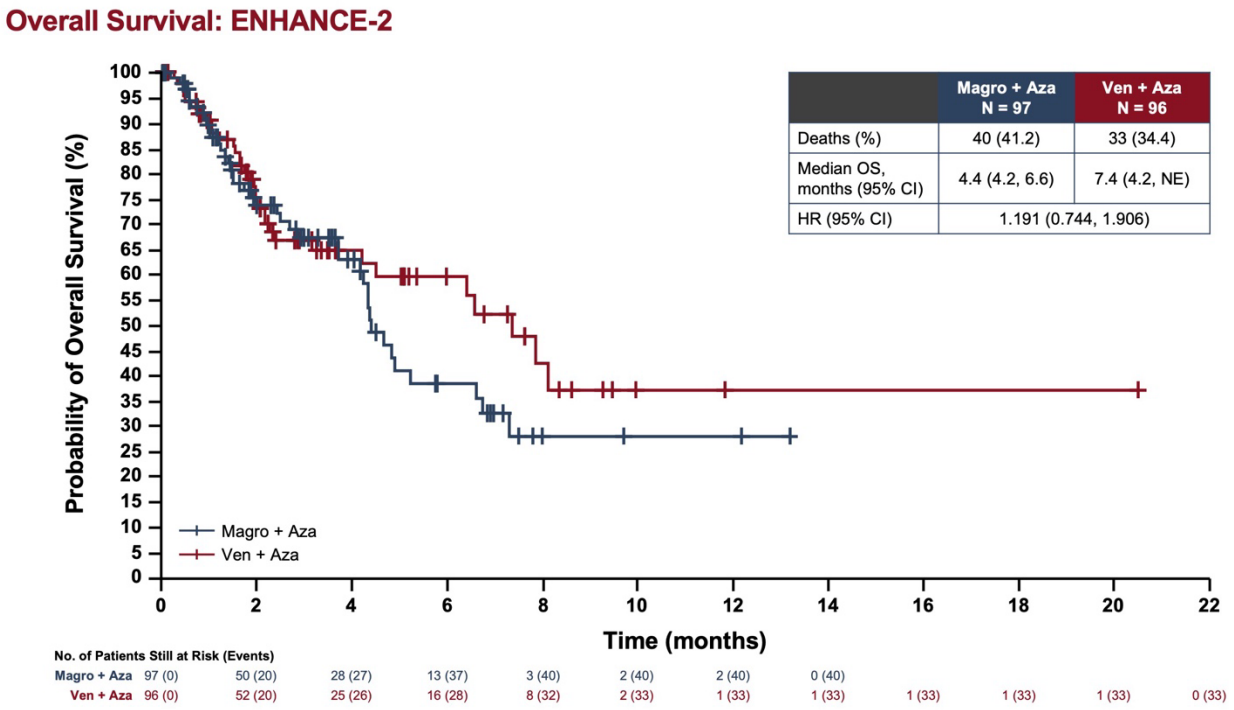
Magro + Aza	268 (0)	242 (21)	216 (44)	200 (58)	160 (78)	138 (85)	113 (100)	101 (100)	87 (120)	69 (124)	47 (131)	32 (135)	18 (138)	12 (138)	4 (138)	0 (138)
Placebo + Aza	271 (0)	255 (15)	242 (28)	224 (44)	189 (55)	152 (74)	127 (87)	113 (100)	90 (111)	67 (114)	47 (117)	30 (123)	18 (123)	9 (123)	3 (123)	1 (123)	0 (124)

The complete response rate was 21.3% in the magrolimab-containing arm, and 24.7% in the control arm. Objective response was 53.5% in the magrolimab-containing arm and 57.8% in the control arm.

There was a 14% increase of severe grade 3-5 adverse events (92.8% vs 78.4%, magrolimab vs control arm). The incidence of serious adverse events was 71.9% compared to 51.5% in the control arm. The rate of fatal adverse events was 15.2% compared to 9.5% in the control arm. The following non-disease progression causes of deaths were identified in the magrolimab arm: febrile neutropenia, acute myocardial infarction, cardiac arrest, coronary artery disease, ventricular tachycardia, gastrointestinal hemorrhage, gastrointestinal ischemia, multiple organ dysfunction syndrome, pneumonia, sepsis, infective arthritis, COVID-19, influenza, neutropenic sepsis, aspiration pneumonia, bacterial pneumonia, septic shock, vascular procedure complication, cerebral hemorrhage, mental status changes, acute kidney injury, respiratory failure, death and sudden death.

ENHANCE-2

ENHANCE-2 is a phase 3, randomized, open-label, controlled trial of azacitidine with magrolimab compared to azacitidine with venetoclax in patients with untreated acute myeloid leukemia with mutated TP53. The study enrolled 238 patients in total, with 193 patients appropriate for non-intensive therapy randomized 1:1 between azacitidine with magrolimab and azacitidine with venetoclax. This was the primary analysis population. Using a data cutoff date of 11 August 2023, a complete evaluation of safety and efficacy was performed. The median survival follow up was 2 months. For overall survival analysis of the primary analysis population, there were 40 deaths on the magrolimab-containing arm and 33 deaths on the control arm. 58.8% were censored in the magrolimab-containing arm and 65.6% were censored in the control arm. The hazard ratio of magrolimab-azacitidine arm compared to the control arm was 1.191 (95% CI 0.744, 1.906), increasing the risk of death on average by 19% compared to the control arm. The study also randomized 45 patients appropriate for intensive therapy to azacitidine with magrolimab and 7 plus 3 chemotherapy, and there were 7 deaths in the magrolimab-arm and 5 deaths in the intensive chemotherapy arm.

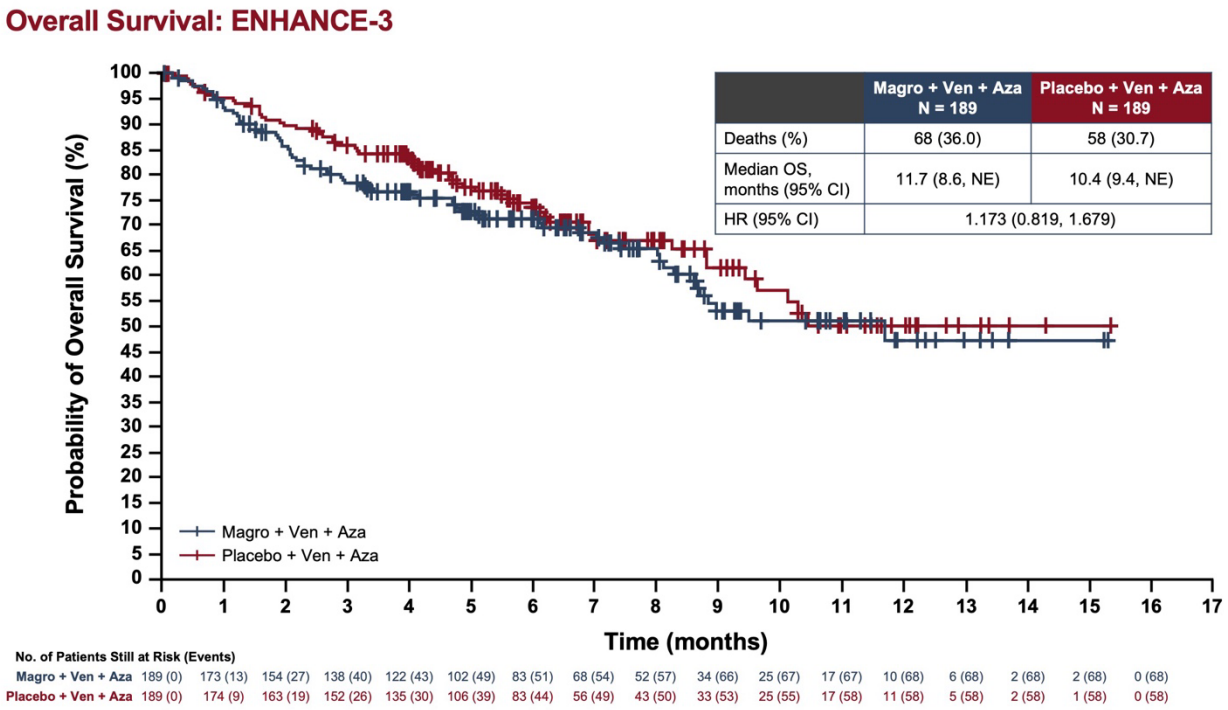


In the primary analysis population, the complete response rate was 7.2% in the magrolimab-containing arm and 15.6% in the control arm.

In the primary analysis population, there was a similar incidence of increase of severe grade 3-5 adverse events (92.0% vs 93.6%, magrolimab vs control arm). The incidence of serious adverse events was 78.4% compared to 76.9% in the control arm. The rate of fatal adverse events was 17.0% compared to 20.5% in the control arm. In all patients treated with magrolimab, the following fatal adverse events were reported in the study: cardiac failure, supraventricular tachycardia cardio-respiratory arrest, disease progression, multiple organ dysfunction syndrome, hemophagocytic lymphohistiocytosis, pneumonia, sepsis, septic shock, infection, encephalopathy, chronic kidney disease, and pneumonitis.

ENHANCE-3

ENHANCE-3 is a phase 3, randomized, double-blinded, controlled trial of azacitidine and venetoclax, with and without magrolimab in patients with untreated acute myeloid leukemia unfit for intensive therapy. Using a data cutoff date of 15 December 2023, a complete evaluation of safety and efficacy was performed. There were 378 randomized patients included in the analysis. The median follow up was 5.7 months in the magrolimab-containing arm, and 5.8 months in the control arm. For overall survival, there were 68 deaths on the magrolimab-containing arm and 58 deaths on the control arm. 64.0% were censored in the magrolimab-containing arm and 69.3% were censored in the control arm. The hazard ratio of magrolimab arm compared to the control arm was 1.173 (95% CI 0.819, 1.679), increasing the risk of death by 17% compared to the control arm.



The complete response rate was 39.7% in the magrolimab-containing arm, and 42.9% in the control arm.

There was a similar incidence of severe grade 3-5 adverse events (95.8% vs 96.2%, magrolimab vs control arm). The incidence of serious adverse events was 72.5% compared to 71.2% in the control arm. There was an 8% increase in the incidence of adverse events leading to death in the magrolimab-containing arm (18.5% vs 10.9%). The following non-disease progression causes of deaths were identified in the magrolimab arm: febrile neutropenia, acute myocardial infection, cardiogenic shock, enteritis, gastrointestinal hemorrhage, multiple organ dysfunction syndrome, pneumonia, sepsis, septic shock, pulmonary sepsis, abdominal sepsis, liver abscess, staphylococcal sepsis, stenotrophomonas sepsis, fall, chronic kidney disease, respiratory failure, and acute respiratory failure.