STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 3, Randomized, Open-Label Study Evaluating the Safety and Efficacy of Magrolimab in Combination with Azacitidine versus Physician's Choice of Venetoclax in Combination with Azacitidine or Intensive Chemotherapy in Previously Untreated Patients with TP53 Mutant Acute Myeloid Leukemia
Name of Test Drug:	Magrolimab
Study Number:	GS-US-546-5857
Protocol Version (Date):	Protocol Amendment 5 (02 November 2023)
Analysis Type:	Final Analysis
Analysis Plan Version:	Version 1.0
Analysis Plan Date:	07 May 2024
Analysis Plan Authors:	PPD

CONFIDENTIAL AND PROPRIETARY INFORMATION

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LIST OF ABBREVIATIONS

ADA	anti-drug antibody
AE	adverse event
ALT	alanine aminotransferase
ALP	alkaline phosphatase
AML	acute myeloid leukemia
AST	aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
BLQ	below the limit of quantitation
BMI	body mass index
BSA	body surface area
CI	confidence interval
COVID-19	coronavirus disease 2019
CR	complete remission
CRF	case report form
CRh	complete remission with partial hematologic recovery
CRi	complete remission with incomplete count recovery
CRMRD-	complete remission without minimal residual disease
$CR_{MRD+/UNK}$	complete remission with positive or unknown minimal residual disease
CSR	clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
CV	coefficient of variation
DCR	duration of complete remission
DMC	Data Monitoring Committee
DOR	duration of response
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
EFS	event-free survival
ELN	European Leukemia Net
EORTC QLQ-C30	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
EQ-5D-5L	5-Level EuroQol 5 Dimensions
EQ VAS	EQ visual analogue scale
EOT	end of treatment
ET	early termination
GHS/QoL	Global Health Status/Quality of Life
Hb	hemoglobin
HiDAC	high-dose Cytarabine
HLT	high-level term
HLGT	high-level group term

HRQoL	health-related quality of life
IA	Interim analysis
ICH	International Conference on Harmonization
ID	identification
IRR	infusion related reaction
IRT	interactive response technology
ITT	Intent-to-Treat
IWG	International Working Group
LLT	lower-level term
LOQ	limit of quantitation
MDS	myelodysplastic syndrome
MedDRA	Medical Dictionary for Regulatory Activities
MLFS	morphologic leukemia-free state
MRD	minimal residual disease
MST	MedDRA Search Term
ORR	objective response rate
OS	overall survival
PR	partial remission
PRO	patient-reported outcome
PGIC	Patient Global Impression of Change
PGIS	Patient Global Impression of Severity
PK	pharmacokinetic
PT	preferred term
Q1, Q3	first quartile, third quartile
RBC	red blood cell
SAE	serious adverse event
SAP	statistical analysis plan
SCT	stem cell transplant
StD	standard deviation
SE	standard error
SI (units)	international system of units
SMQ	Standardised MedDRA Queries
SOC	system organ class
TE	treatment-emergent
TEAE	treatment-emergent adverse event
TFLs	tables, figures, and listings
TTD	time to first deterioration
TTR	time to response
ULN	upper limit of normal
WHO	World Health Organization

1. INTRODUCTION

This statistical analysis plan (SAP) describes the statistical analysis methods and data presentations to be used in tables, figures, and listings (TFLs) of the final analyses for Study GS-US-546-5857. This SAP is based on the study protocol amendment 5 dated 02 November 2023. Any changes made after the finalization of the SAP will be documented in the clinical study report (CSR).

1.1. Study Objectives

The primary objective of this study is as follows:

- To compare the efficacy of magrolimab + azacitidine versus venetoclax + azacitidine in patients with previously untreated *TP*53 mutant acute myeloid leukemia (AML) who are appropriate for non-intensive therapy as measured by overall survival (OS).

The secondary objectives of this study are as follows:

- To compare the efficacy of magrolimab + azacitidine versus physician's choice of venetoclax + azacitidine or 7 + 3 chemotherapy in all patients with previously untreated *TP*53 mutant AML as measured by OS.
- To compare the efficacy of magrolimab + azacitidine versus physician's choice of venetoclax + azacitidine or 7 + 3 chemotherapy in all patients as measured by event-free survival (EFS).
- To compare the efficacy of magrolimab + azacitidine versus physician's choice of venetoclax + azacitidine or 7 + 3 chemotherapy as measured by rate of complete remission (CR) within 2 months of treatment for patients treated with 7 + 3 chemotherapy and within 6 months of treatment for other patients.
- To compare the efficacy of magrolimab + azacitidine versus physician's choice of venetoclax + azacitidine or 7 + 3 chemotherapy as measured by rate of CR without minimal residual disease (CR_{MRD-}) within 2 months of treatment for patients treated with 7 + 3 chemotherapy and within 6 months of treatment for other patients.
- To compare the efficacy of magrolimab + azacitidine versus physician's choice of venetoclax + azacitidine or 7 + 3 chemotherapy in all patients as measured by the rate of CR + complete remission with partial hematologic recovery (CRh) within 2 months of treatment for patients treated with 7 + 3 chemotherapy and within 6 months of treatment for other patients.
- To evaluate the duration of complete remission (DCR) in patients who achieved CR within 6 months of treatment with magrolimab + azacitidine or venetoclax + azacitidine, or within 2 months of 7 + 3 chemotherapy.
- To evaluate the duration of CR + CRh in patients who achieved CR or CRh within 6 months of treatment with magrolimab + azacitidine or venetoclax + azacitidine, or within 2 months of 7 + 3 chemotherapy.

- To assess the safety and tolerability of magrolimab + azacitidine versus physician's choice of venetoclax + azacitidine or 7 + 3 chemotherapy.

- To evaluate the pharmacokinetics (PK) and immunogenicity of magrolimab.

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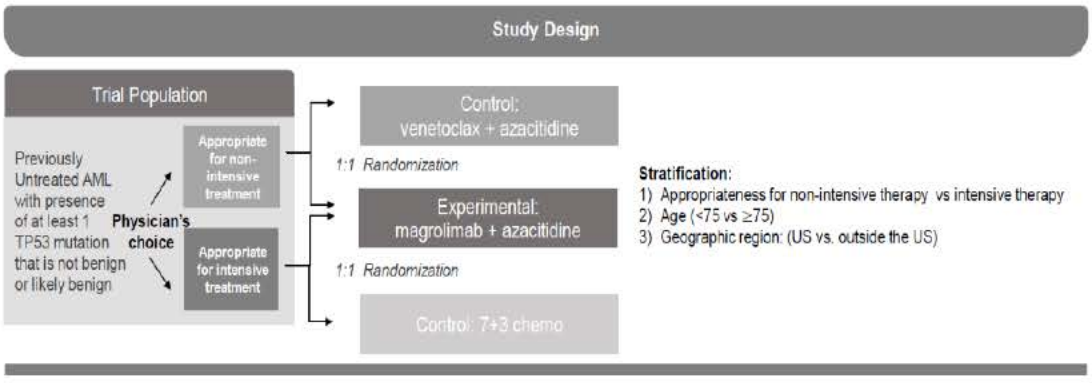
[redacted]

1.2. Study Design

This is a Phase 3, randomized, open-label, multicenter study comparing magrolimab + azacitidine versus physician's choice of venetoclax + azacitidine or 7+3 chemotherapy in patients with previously untreated *TP53* mutant AML. Approximately 346 patients will be randomized in 1:1 ratio to receive either magrolimab + azacitidine (experimental arm) or physician's choice of venetoclax + azacitidine or 7 + 3 chemotherapy (control arm). Randomization will be stratified by 3 factors:

- appropriateness for non-intensive therapy versus intensive therapy
- age (< 75 years, ≥ 75 years)
- geographic region (United States [US], outside the US)



The primary endpoint is OS in the stratum of patients appropriate for non-intensive therapy. The primary analysis of the OS will be conducted when 171 deaths have occurred in the stratum of patients appropriate for non-intensive therapy. An interim futility analysis and an interim superiority analysis will be conducted separately after approximately 69 and 128 deaths (40% and 75% of the expected 171 deaths, respectively) in the stratum of patients appropriate for non-intensive therapy have occurred.

The study met futility based on an adhoc analysis with futility assessment conducted in August 2023, and sites were informed of the outcome and sponsor's decision to terminate the study earlier than planned in a communication in September 2023. If an investigator believes that continued treatment with magrolimab + azacitidine is in the best interest of their patient(s), Gilead will continue to provide study drug, with a reduced schedule of assessments, pending final study closure. In February 2024, a planned interim analysis of the Phase 3 ENHANCE-3 study demonstrated futility in OS with an increased risk of death in the magrolimab-treatment arm. Based on the results, as well as data from the clinical study in higher-risk MDS (ENHANCE) and this study where the interim analyses also demonstrated futility with an increased risk of death in the magrolimab-treatment arm, FDA placed all magrolimab studies in MDS and AML, including related expanded access programs, on a full clinical hold. Gilead will not pursue further development of magrolimab in hematologic cancers. All AML patients who were remaining on magrolimab in this study have discontinued magrolimab and will leave study.

The study treatments within each arm are as follows:

Table 1-1. Dosing and Schedule for Magrolimab and Azacitidine Experimental Arm

Drug/Dose/Route	Dose Schedule (Day per 28-day Cycle)		
	Cycle 1	**Cycle 2**	**Cycle 3+**
Azacitidine 75 mg/m^2 SC or IV[a]	Days 1–7 or Days 1–5 and 8, 9[b]	Days 1–7 or Days 1–5 and 8, 9[b]	Days 1–7 or Days 1–5 and 8, 9[b]
Magrolimab Administration			
Magrolimab 1 mg/kg IV (over 3 hours)	Days 1, 4		
Magrolimab 15 mg/kg IV (over 3 hours)	Day 8		
Magrolimab 30 mg/kg IV (over 2 hours)	Days 11 and 15, and then QW x 5 weekly 30 mg/kg dose		
Magrolimab 30 mg/kg IV (over 2 hours)	Q2W beginning 1 week after the 5 weekly 30 mg/kg dose		

IV = intravenous; PO = orally; Q2W = every 2 weeks; QW = once a week; SC = subcutaneous
a Azacitidine administered per region-specific labeling.
b Or any other alternative schedule, as long as the 7 doses of azacitidine of the cycle are administered within 9 consecutive days.

Table 1-2. Dosing and Schedule for Venetoclax and Azacitidine Control Arm

Control Arm	Drug/Dose/Route	Dose Schedule (Day per 28-day Cycle)		
		Cycle 1	Cycle 2	Cycle 3+
Venetoclax + Azacitidine	Venetoclax 100 mg oral	Day 1	—	—
	Venetoclax 200 mg oral	Day 2	—	—
	Venetoclax 400 mg oral	Day 3 and daily thereafter	Daily	Daily
	Azacitidine 75 mg/m^2 SC or IV[a]	Days 1–7 or Days 1-5 and 8-9[b]	Days 1–7 or Days 1-5 and 8-9[b]	Days 1–7 or Days 1-5 and 8-9[b]

IV = intravenous; SC = subcutaneous
a Azacitidine administered per region-specific labeling.
b Or any other alternative schedule, as long as the 7 doses of azacitidine of the cycle are administered within 9 consecutive days.

Table 1-3. Dosing and Schedule for 7 + 3 Chemotherapy Control Arm

Control Arm (7+3)	Drug/Dose/Route	7 + 3 Induction	5 + 2 Induction, if needed (after C1D15 bone marrow assessment)
Induction	Daunorubicin 60 mg/m^2 IVP or Idarubicin 12 mg/m^2 IV	Days 1–3	Days 1-2
	Cytarabine 100 or 200 mg/m^2 CI	Days 1–7	Days 1–5
Consolidation	Cytarabine (HiDAC) 1500 or 3000 mg/m^2 IV[a]	Every 12 hours on Days 1, 3, and 5 (up to 4 cycles)	
	Steroidal Eye Drops	As per institutional standard	

C1D15 = Cycle 1 Day 15; CI = continuous infusion; IV = intravenous; IVP = intravenous peripheral
a In some cases, patients ≥ 60 years of age can receive 1000 mg/m^2 based on local practice.

For the experimental arm and the control arm venetoclax + azacitidine, cycle length is 28 days, and all patients will continue on study treatment until disease progression, relapse, loss of clinical benefit, or unacceptable toxicities occur.

For patients treated with 7 + 3 chemotherapy (with or without 5 + 2 chemotherapy as indicated), induction followed by up to 4 cycles of consolidation with high-dose cytarabine (HiDAC) should be administered unless study treatment discontinuation criteria are met.

Patients will be discontinued from study treatment prior to starting stem cell transplant (SCT). No cross-over between arms is allowed.

Treatment with azacitidine as SOC is recommended for a minimum of 6 cycles. Therefore, in this study, for the patients in the magrolimab + azacitidine or venetoclax + azacitidine treatment arms, those without evidence of disease progression (including relapse), loss of clinical benefit, or unacceptable toxicity should continue study treatment. For those in the 7 + 3 chemotherapy treatment arm, treatment should continue until the end of the induction cycle(s).

Treatment with magrolimab or venetoclax as single agent is not permitted.

Clinical response will be assessed using the guidelines in the study protocol Appendix 6 which are based primarily on European Leukemia Net (ELN) AML 2017 recommendation and the 2003 International Working Group (IWG) AML response criteria with modifications. Response assessments will be performed in conjunction with bone marrow assessments, according to the schedule of assessments (Appendix 1). Accompanying laboratory results ± 2 weeks from the protocol-specified bone marrow efficacy assessment can be used to support an efficacy assessment, but peripheral blood smears for blasts should be done on the day of the bone marrow assessments. Response assessments for magrolimab + azacitidine and venetoclax + azacitidine are scheduled at Cycle 1 Day 28, Cycle 2 Day 28, Cycle 4 Day 28, Cycle 6 Day 28, and then at the end of every 3 cycles thereafter during study treatment. For patients who receive control treatment with 7 + 3 (5 + 2) chemotherapy, response assessments will be performed as summarized in the schedule of assessments in Appendix 1. These supporting laboratory results will be entered into the eCRF. If a patient achieves a CR, subsequent bone marrow assessments are still required to be performed as per the schedule of assessments in Appendix 1.

Response assessment will be obtained at the end of treatment (EOT) visit, unless a prior response assessment has been performed within the last 30 days or progressive disease has been documented, or if patient continues on long-term follow-up. Response assessments should continue during long-term follow-up approximately every 12 weeks until progressive disease is documented or start of a new anti-AML therapy (excluding SCT and maintenance). For patients who come off the study treatment to receive a SCT, follow-up for response assessment and collection of bone marrow biopsy/aspirate results will continue every 12 weeks from the date of SCT, until documented disease progression or relapse or initiation of new anti-AML therapy (excluding maintenance therapy) occurs. Then patients will be observed for survival until death, withdrawal of consent, loss to follow-up, or the end of the study, whichever occurs first.

All patients will be followed for survival until death. For any patient who dies during this follow-up period, the immediate cause of death must be reported to the sponsor.

The study met futility based on an adhoc analysis with futility assessment conducted in August 2023, and sites were informed of the outcome and sponsor's decision to early terminate the study in a communication in September 2023. All patients who discontinue study treatment for any reason will not be followed for response or survival.

1.3. Sample Size and Power

Based on data from Study 5F9005, which enrolled 47 *TP53* mutant AML patients treated with magrolimab + azacitidine with a median OS of 12.9 months {Sallman 2020}, and from studies for venetoclax in combination with hypomethylating agents that have shown a median OS ranging from 5.2 to 7.2 months in *TP53* mutant AML patients {DiNardo 2019, Kim 2020}, it is assumed that administration of magrolimab + azacitidine to study patients will result in a median OS of approximately 9.77 months, improved from a median OS of 6.35 months in patients treated with venetoclax + azacitidine or 7 + 3 chemotherapy. This corresponds to an OS hazard ratio (HR) of 0.65.

It is assumed that the duration of OS is exponentially distributed in each of the 2 arms. With an HR equal to 1 under the null hypothesis of no difference between the 2 treatment arms, an HR of 0.65 under the alternative hypothesis of superiority of the magrolimab + azacitidine, a planned interim futility analysis and an interim superiority analysis when 40% and 75% of the OS events required for the primary analysis are observed respectively, a total of 171 OS events (deaths) in the stratum of patients appropriate for non-intensive therapy is required at the primary analysis to achieve a power of 79.7% based on a log-rank test with an overall 1-sided significance level of 0.025; approximately 234 deaths may be observed in all patients when 171 events occur in the stratum of patients appropriate for non-intensive therapy. That provides a power of 90.4% for the OS test in all patients based on the log-rank test.

The study will enroll a minimum of 228 patients appropriate for non-intensive therapy to ensure adequate events (171 deaths) for the primary endpoint analysis. The study enrollment may stop after 228 patients in the non-intensive therapy group or approximately 346 of all patients are enrolled, whichever occurs later. The study duration and the total number of patients to be enrolled will depend on the prevalence of patients appropriate for non-intensive therapy in the overall population. When the enrollment of the required number of all patients finishes later than that of patients in the non-intensive therapy group, assuming a planned accrual period of 23 months, a study duration of 27 months, and an expectation that 10% of patients are likely to drop out by the end of study (annual dropout rate 4.8% assuming time to drop-out is exponentially distributed), approximately 173 patients in the experimental arm and 173 patients in the control arm (approximately 346 total) are to be enrolled. The study met futility based on an adhoc analysis with futility assessment conducted in August 2023, and sites were informed of the outcome and sponsor's decision to terminate the study earlier than planned in a communication in September 2023. No further patients were enrolled.

2. TYPE OF PLANNED ANALYSIS

2.1. Interim Analyses

2.1.1. Data Monitoring Committee (DMC) Analysis

An external multidisciplinary data monitoring committee (DMC) will review the progress of the study and perform interim reviews of safety data in order to protect patient welfare and preserve study integrity. To ensure the best interests of the patients, the DMC will make recommendations to the sponsor if the nature, frequency, and severity of adverse effects associated with the study treatment warrant the early termination of the study, the continuation of the study, or the continuation of the study with modifications.

In addition, the DMC will meet after approximately 69 and 128 OS events in the stratum of patients appropriate for non-intensive therapy have occurred to review the results from the planned interim analyses, as specified in Section 2.1.2 and 2.1.3. Based on the pre-specified futility and superiority rules, the DMC may make recommendations to Gilead on whether the study should be terminated early due to futility, should be stopped due to overwhelming efficacy, or should continue as planned.

The DMC's specific activities will be defined by a mutually agreed charter, which will define the DMC's membership, conduct, and meeting schedule.

The DMC's role and responsibilities and the scope of analysis to be provided to the DMC will be defined by a mutually agreed charter, which defines the DMC's membership, conduct, and meeting schedule.

While the DMC will be asked to advise Gilead regarding future conduct of the study, including possible early study termination, Gilead retains final decision-making authority on all aspects of the study.

2.1.2. Interim Futility Analysis

An interim analysis for futility is planned. This analysis will be performed after approximately 69 deaths (40% of the expected 171 OS events) in the stratum of patients appropriate for non-intensive therapy have occurred. The analysis will include a stratified log-rank test for OS in the stratum of patients appropriate for non-intensive therapy and will be reviewed by the DMC. A non-binding futility rule with a boundary HR = 1.1 will be implemented. The DMC may make a recommendation to terminate the study for futility if the observed HR for the OS in patients appropriate for non-intensive therapy is larger than 1.1. When the true OS HR in patients appropriate for non-intensive therapy is 0.74, the probability of observing HR > 1.1 at the interim analysis is less than 5%. Additional details are provided in Appendix 2.

2.1.3. Interim Efficacy Analysis for Superiority

An interim efficacy analysis for OS superiority will be performed after approximately 128 deaths (75% of the expected 171 OS events) in the stratum of patients appropriate for non-intensive therapy have occurred, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized. The Lan-DeMets approach with O-Brien-Fleming type alpha spending function will be used to define the stopping boundaries for the primary endpoint OS in the stratum of patients appropriate for non-intensive therapy. The DMC will review unblinded interim analyses results and make recommendations per prespecified efficacy boundaries (refer to Table 2-1) to Gilead team as outlined in the DMC charter.

To strongly control the overall Type I error across the testing of the primary and key secondary efficacy endpoints, a hierarchical testing strategy will be performed at the interim analysis for superiority and the primary analysis, respectively. The overall study-wide type I error is one-sided 0.025. An administrative one-sided type I error of 0.0001 will be spent for the interim futility analysis to protect the integrity of the study. As a result, the primary efficacy endpoint, OS in patients appropriate for non-intensive therapy, will be tested for superiority first at a one-sided significance level of 0.0249. If the OS interim results indicate superiority, analysis of key secondary efficacy endpoints with a one-sided significance level of 0.0249 will be performed in the following order:

- OS in all patients
- EFS in all patients
- Rate of CR within 6 months of treatment (2 months for patients receiving 7 + 3 chemotherapy)
- Rate of CR_{MRD-} within 6 months of treatment (2 months for patients receiving 7 + 3 chemotherapy)
- Rate of CR + CRh within 6 months of treatment (2 months for patients receiving 7 + 3 chemotherapy)

A given hypothesis can only be tested and declared statistically significant if all previous hypotheses tested in the hierarchy are statistically significant. If the superiority test is failed at certain endpoint, all the hypothesis tests that follow thereafter will be considered descriptive with nominal significance (p-values) reported.

The Lan-DeMets approach with O'Brien-Fleming type alpha spending function will be used to account for multiplicity introduced by including the OS interim efficacy analysis for superiority. The stopping boundaries for the analyses of the primary endpoint OS in the stratum of patients appropriate for non-intensive therapy are provided in Table 2-1.

Table 2-1. Stopping Boundaries for Efficacy Analyses for Superiority

Efficacy Analysis	Events (%[a])	Stopping Boundary	
		HR	1-Sided P-Value
IA	128 (75%)	0.661	0.010
Primary Analysis	171 (100%)	0.735	0.022

HR = hazard ratio; IA = interim analysis; OS = overall survival
a Information fraction = number of events/total number of events × 100

For each key secondary endpoint, an O'Brien-Fleming type of boundary will be derived based on the information fraction defined at the interim efficacy analysis and the remaining type I error, respectively, per Table 2-2.

Table 2-2. Definition of Information Fraction

Secondary Endpoint	Information Fraction at the Interim Analysis
OS in all patients	75%, same with that of primary efficacy endpoint
EFS in all patients	75%, same with that of primary efficacy endpoint
Rate of CR within 6 months of treatment (2 months for patients receiving 7 + 3 chemotherapy)	Proportion of patients who have at least 7 months follow-up since randomization (3 months for patients receiving 7 + 3 chemotherapy)
Rate of CR_{MRD-} within 6 months of treatment (2 months for patients receiving 7 + 3 chemotherapy)	Proportion of patients who have at least 7 months follow-up since randomization (3 months for patients receiving 7 + 3 chemotherapy)
Rate of CR + CRh within 6 months of treatment (2 months for patients receiving 7 + 3 chemotherapy)	Proportion of patients who have at least 7 months follow-up since randomization (3 months for patients receiving 7 + 3 chemotherapy)

CR = complete remission; CR_h = complete remission with partial hematologic recovery; CR_{MRD-} = complete remission without minimal residual disease; EFS = event-free survival; OS = overall survival;

If the OS interim analysis results do not meet the efficacy boundary for superiority, then the study will continue as planned. The study met futility based on an adhoc analysis with futility assessment conducted in August 2023, and sites were informed of the outcome and sponsor's decision to early terminate the study in a communication in September 2023. The planned interim analysis for superiority is no longer required.

2.2. Primary Analysis

If the null hypothesis on the primary endpoint of OS in the stratum of patients appropriate for non-intensive therapy is not rejected in the planned interim efficacy analysis, the primary efficacy analysis will be conducted when 171 deaths have occurred in the stratum of patients appropriate for non-intensive therapy. The analysis will be conducted after all outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized for the analysis. The analysis of the primary endpoint OS in the stratum of patients appropriate for non-intensive therapy will be used to evaluate efficacy of magrolimab +

azacitidine compared with venetoclax + azacitidine in the patient population and will serve as the final analysis for this endpoint. The corresponding stopping boundary and the hierarchical hypothesis testing are specified in Section 2.1.3. If the null hypothesis of the primary endpoint OS is rejected in the interim efficacy analysis, the primary analysis timing will be determined by the maturity of the key secondary endpoints that have not been rejected in the interim analysis. The study met futility based on an adhoc analysis with futility assessment conducted in August 2023, and sites were informed of the outcome and sponsor's decision to terminate the study earlier than planned in a communication in September 2023. The planned primary analysis is no longer required.

2.3. Final Analysis

The final analysis of the data will be performed after all patients have completed the study, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized. The analysis of the primary endpoint of OS will be conducted at this time and will be descriptive in nature.

The study met futility based on an adhoc analysis with futility assessment conducted in August 2023, and sites were informed of the outcome and sponsor's decision to terminate the study earlier than planned in a communication in September 2023. By the time the sponsor made the decision to end the study, 257 patients have been randomized.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

Analysis results will be presented using descriptive statistics. For categorical variables, the number and percentage of patients in each category will be presented; for continuous variables, the number of patients (n), mean, standard deviation (StD) or standard error (SE), median, first quartile (Q1), third quartile (Q3), minimum, and maximum will be presented.

By-subject listings will be presented for all patients in the Intent-to-Treat (ITT) Analysis Set and sorted by treatment group, subject ID number, visit date, and time (if applicable). Data collected on log forms, such as AEs, will be presented in chronological order within the subject. Age, sex at birth, race, and ethnicity will be included in the listings, as space permits.

3.1. Analysis Sets

Analysis sets define the patients to be included in an analysis. Analysis sets and their definitions are provided in this section. The analysis set will be identified and included as a subtitle of each table, figure, and listing.

For each analysis set, the number and percentage of patients eligible for inclusion will be summarized by treatment group.

3.1.1. Intent-to-Treat (ITT) Analysis Set

The ITT Analysis Set includes all patients who were randomized in the study, with treatment assignment designated according to the treatment arm the subject is randomized to. This is the primary analysis set for efficacy analyses, unless otherwise specified.

3.1.2. Safety Analysis Set

The Safety Analysis Set includes all patients who took at least 1 dose of any study treatment, with treatment assignment designated according to the actual treatment received. This is the primary analysis set for safety analyses.

3.1.3. Pharmacokinetic Analysis Set

The Pharmacokinetic (PK) Analysis Set will include all randomized patients who took at least one dose of magrolimab and have at least 1 measurable (non-BLQ numeric values) post-treatment serum concentration of magrolimab. This is the primary analysis set for all PK analyses.

3.1.4. Immunogenicity Analysis Set

The Immunogenicity Analysis Set will include all randomized patients who received at least one dose of magrolimab and had at least one evaluable anti-magrolimab antibody test result.

3.2. Subject Grouping

For analyses based on the ITT Analysis Set, patients will be grouped according to the treatment to which they were randomized. For analyses based on the Safety Analysis Set, patients will be grouped according to the actual treatment received. The actual treatment received will differ from the randomized treatment only when their actual treatment differs from randomized treatment for the entire treatment duration.

For the PK Analysis Set and the Immunogenicity Analysis Set, patients will be grouped according to the actual treatment they received.

3.3. Strata and Covariates

Patients will be randomized in a 1:1 ratio to treatment arms via an integrated response technology (IRT) with a stratified randomization schedule. Stratification will be based on the following variables:

- appropriateness for non-intensive therapy versus intensive therapy
- age (< 75 years, ≥ 75 years)
- geographic region (United States [US] sites, outside the US sites)

If there are discrepancies in stratification factor values between the IRT and the clinical database, the values recorded in the clinical database will be used for analyses.

Efficacy endpoints will be evaluated using stratification factors as covariates or stratification variables for analyses when applicable, as specified in Section 6. If there is an imbalance in presumed prognostic baseline characteristics between treatment groups, efficacy evaluations may be performed that include these baseline values in efficacy analysis models as covariates; these evaluations will be considered as sensitivity analyses.

3.4. Examination of Subject Subgroups

Subgrouping of patients based on randomization stratification factors may be explored for subgroup analyses. The primary and selected secondary efficacy endpoints (defined in Section 6) may be examined using the following subgroups:

- appropriateness for non-intensive therapy versus intensive therapy
- age (< 75 years, ≥ 75 years)
- geographic region (US sites, outside the US sites)

If there is an imbalance between treatment groups in presumed prognostic baseline characteristics that are not stratification factors, subgroupings based on these imbalanced baseline characteristics may also be explored for analysis of the primary endpoint and key secondary efficacy endpoints.

3.5. Adjustment for Multiplicity

The adjustment for multiplicity (if applicable) is specified in Section 2.1.3. As the study is terminated early due to futility, no multiplicity adjustment is implemented.

3.6. Missing Data and Outliers

3.6.1. Missing Data

In general, missing data will not be imputed unless methods for handling missing data are specified. Exceptions are presented in this document.

Imputation rules for missing date of birth are described in Section 3.7. The handling of missing or incomplete dates for date of death and the start date of new anti-AML therapy in Section 6.2.1, for AE onset in Section 7.1.5.2, and for prior and concomitant medications in Section 7.4. Imputation rules adopted in the efficacy analyses are specified in Section 6.

3.6.2. Outliers

Outliers will be identified during the data management and data analysis process, but no sensitivity analyses will be conducted. All data will be included in the data analysis.

3.7. Data Handling Conventions and Transformations

The following conventions will be used for the imputation of date of birth when it is partially missing or not collected:

- If only month and year of birth is collected, then "15" will be imputed as the day of birth
- If only year of birth is collected, then "01 July" will be imputed as the day and month of birth
- If year of birth is missing, then date of birth will not be imputed

In general, age collected at the randomization (in years) will be used for analyses and presented in listings. If age at randomization is not available for a subject, then age derived based on date of birth and the randomization date will be used instead. For screen failures or unrandomized patients, the date the first informed consent was signed will be used for the age derivation. Age required for longitudinal and temporal calculations and analyses (eg, estimates of creatinine clearance, age at date of AE) will be based on age derived from date of birth and the date of the measurement or event, unless otherwise specified.

Non-PK data that are continuous in nature but are less than the lower limit of quantitation (LOQ) or above the upper LOQ will be imputed as follows:

- A value that is 1 unit less than the lower LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "< x" (where x is considered the lower LOQ). For example, if the values are reported as < 50 and < 5.0, values of 49 and 4.9, respectively, will

be used to calculate summary statistics. An exception to this rule is any value reported as < 1 or < 0.1, etc. For values reported as < 1 or < 0.1, a value of 0.9 or 0.09, respectively, will be used to calculate summary statistics.

- A value that is 1 unit above the upper LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "> x" (where x is considered the upper LOQ). Values with decimal points will follow the same logic as above.

- The lower or upper LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "≤ x" or "≥ x" (where x is considered the lower or upper LOQ).

If methods based on the assumption that the data are normally distributed are not adequate, analyses may be performed on transformed data or nonparametric analysis methods may be used, as appropriate.

3.8. Analysis Visit Windows

3.8.1. Definition of Study Day

Study day will be calculated from the first dosing date of any study drug, which is the earliest dose date of magrolimab, venetoclax, azacitidine, or 7+3 chemotherapy and derived as follows:

- For postdose study days: Assessment Date – First Dosing Date + 1

- For days prior to the first dose: Assessment Date – First Dosing Date

Therefore, study day 1 is the day of first dose of any study drug administration. If the subject is randomized but not dosed, the randomization date will be study day 1.

3.8.2. Analysis Visit Windows

Subject visits might not occur on protocol-specified days. Therefore, for the purpose of analysis, observations will be assigned to analysis windows. The analysis windows for laboratory analytes are provided in Table 3-1 to Table 3-2.

Table 3-1. Analysis Visit Windows for Hematology Labs

Analysis Visit	Nominal Study Visit or Study Day	Visit Window Study Day[a]	
		Lower Limit	Upper Limit
Baseline			1[b]
Day 1 post-dose	Set 1 Day 1, post-dose Cycle 1 Day 1, post-dose Unscheduled[d], post-dose	1[c]	1
Day 2	Cycle 1 Day 2 Induction Cycle 1 Day 2	2	2
Day 3	Cycle 1 Day 3	3	3
Day 4 pre-dose	Set 1 Day 4, pre-dose Cycle 1 Day 4 Induction Cycle 1 Day 4 Unscheduled[e], pre-dose	4	4
Day 4 post-dose	Set 1 Day 4, post-dose Unscheduled[f], post-dose	NA	NA
Week 1	8	5	11
Week 2	15	12	18
Week 3	22	19	25
Week 4	29	26	32
Week 5	36	33	39
Week 6	43	40	46
Week 7	50	47	53
Week 8	57	54	63
Week 10	71	64	77
Week xx (every other week from Week 10)	xx*7 + 1	xx*7-6	xx*7+7

a The 1st magrolimab/placebo infusion date is considered as Day 1 in study day calculation if patients are administered magrolimab/placebo.
b On or prior to first magrolimab date/time if the patient is infused with magrolimab, otherwise use first dose date/time of any study drug.
c Post first magrolimab date/time if the patient is infused with magrolimab, otherwise use first dose date/time of any study drug.
d Hemoglobin collected at unscheduled post-dose visit on the same day of or one day after Set 1 Day 1 visit is mapped to Day 1 post-dose.
e Hemoglobin collected at unscheduled pre-dose visit on the same day of Set 1 Day 4 visit is mapped to Day 4 pre-dose.
f Hemoglobin collected at unscheduled post-dose visit on the same day of or one day after Set 1 Day 4 visit is mapped to Day 4 post-dose.

Table 3-2. Analysis Visit Windows for Chemistry Labs

Analysis Visit	Nominal Study Visit or Study Day	Visit Window Study Day	
		Lower Limit	Upper Limit
Baseline			1[a]
Day 1 Post-Dose 6-8 Hour	Cycle 1 Day 1, 6-8 Hour Post-Dose Unscheduled[b], 6-8 Hour post-dose	NA	NA
Day 2 Pre-Dose	Cycle 1 Day 2 Induction Cycle 1 Day 2 Unscheduled	2	2
Day 2 Post-Dose 6-8 Hour	Cycle 1 Day 2, 6-8 Hour Post-Dose Unscheduled[c], 6-8 Hour post-dose	NA	NA
Day 3 Pre-Dose	Cycle 1 Day 3 Unscheduled	3	3
Day 3 Post-Dose 6-8 Hour	Cycle 1 Day 3, 6-8 Hour Post-Dose Unscheduled[d], 6-8 Hour post-dose	NA	NA
Day 4 Pre-Dose	Cycle 1 Day 4 Induction Cycle 1 Day 4 Unscheduled	4	4
Week 1	8	5	11
Week 2	15	12	18
Week 3	22	19	25
Week 4	29	26	32
Week 5	36	33	39
Week 6	43	40	46
Week 7	50	47	53
Week 8	57	54	63
Week 10	71	64	77
Week xx (every other week from Week 10)	xx*7 + 1	xx*7-6	xx*7+7

a On or prior to first dose date/time of any study drug.
b Laboratory records collected at unscheduled 6-8 hour post-dose visit on the same day of or one day after Cycle 1 Day 1 visit is mapped to Day 1 post-dose 6-8 hour.
c Laboratory records collected at unscheduled 6-8 hour post-dose visit on the same day of or one day after Cycle 1 Day 2 visit is mapped to Day 2 post-dose 6-8 hour.
d Laboratory records collected at unscheduled 6-8 hour post-dose visit on the same day of or one day after Cycle 1 Day 3 visit is mapped to Day 3 post-dose 6-8 hour.
e Laboratory records collected at unscheduled 24 hour post-dose visit on the same day of or one day after Cycle 1 Day 3 visit is mapped to Day 3 post-dose 24 hour.

For any data relating to unscheduled visits, the following rules will be implemented:

- An unscheduled visit prior to the first dosing of any study drug will be included in the calculation of the baseline value, if applicable.
- Unscheduled visits after the first dosing of any study drug will be included in determining the maximum postbaseline toxicity grade and anti-magrolimab antibody status.
- Response assessments and patient-reported outcome (PRO) assessments performed at unscheduled visits after the date of randomization will be included in the analyses of the efficacy endpoints and the PRO related endpoints, respectively.

3.8.3. Selection of Data in the Event of Multiple Records in an Analysis Visit Window

If multiple valid, nonmissing measurements exist in an analysis window, records will be chosen based on the following rules if a single value is needed:

- For baseline, the last nonmissing value on or prior to the first dosing date of study drug will be selected, unless specified differently. If there are multiple records with the same time or no time recorded on the same day, the baseline value will be the arithmetic average of the measurements for continuous data, or the measurement with the lowest severity for categorical data.
- For postbaseline values:
  - The record closest to the nominal day for that visit will be selected.
  - If there are 2 records that are equidistant from the nominal day, the later record will be selected.
  - If there is more than 1 record on the selected day, the arithmetic average will be taken for continuous data and the worse severity will be taken for categorical data, unless otherwise specified.

4. SUBJECT DISPOSITION

4.1. Subject Enrollment and Disposition

A summary of subject enrollment will be provided by treatment group for each country, investigator and overall. The summary will present the number and percentage of patients enrolled. For each column, the denominator for the percentage calculation will be the total number of patients analyzed for that column.

A similar enrollment table will be provided by randomization stratum. The denominator for the percentage of patients in the stratum will be the total number of enrolled patients. If there are discrepancies in the value used for stratification assignment between the IRT and the clinical database, the value collected in the clinical database will be used for the summary. A listing of patients with discrepancies in the value used for stratification assignment between the IRT and the clinical database at the time of data finalization will be provided.

The randomization schedule used for the study will be provided as an appendix to the CSR.

A summary of subject disposition will be provided by treatment group. This summary will present the number of patients screened and the number of patients who screen failed, and the number of patients in each of the categories listed below by treatment group:

- ITT Analysis Set
- Safety Analysis Set
- Continuing study treatment (magrolimab+ azacitidine [by therapy appropriateness], venetoclax + azacitidine, intensive chemotherapy)
- Discontinued study treatment (magrolimab+ azacitidine [by therapy appropriateness], venetoclax + azacitidine, intensive chemotherapy) with reasons for discontinuation
- Continuing study (if applicable)
- Discontinued study with reasons for discontinuation

For the status of study drug and study completion and reasons for discontinuation, the number and percentage of patients in each category will be provided. The denominator for the percentage calculation will be the total number of patients in the ITT Analysis Set corresponding to that column.

The following by-subject listing will be provided by subject identification (ID) number in ascending order to support the above summary tables:

- Reasons for study drug discontinuation
- Reasons for study discontinuation

4.2. Extent of Study Drug Exposure and Relative Dose Intensity

Extent of exposure to study drug will be examined by assessing the total duration of exposure to study drug and relative dose intensity. Each variable will be calculated for magrolimab, venetoclax, azacitidine, and the 7+3 (or 5+2) chemotherapy separately. Analyses will be performed separately in the strata of patients appropriate for non-intensive therapy and appropriate for intensive therapy. No formal statistical testing between treatment group is planned.

4.2.1. Duration of Exposure to Study Drug

4.2.1.1. Study Drug: Magrolimab, Venetoclax, and Azacitidine

Total duration of exposure to each study drug (magrolimab, venetoclax, and azacitidine) will be defined for a subject as last dosing date minus first dosing date plus 1 day, regardless of any temporary interruptions in study drug administration, and will be expressed in weeks using up to 1 decimal place (eg, 4.5 weeks).

The total duration of exposure to each study drug will be summarized using descriptive statistics for continuous variables, as well as using the number (i.e., cumulative counts) and percentage of patients exposed for at least the following time periods: 1 day, 1 week, 4 weeks, 6 weeks, 8 weeks, 12 weeks, 16 weeks, 20 weeks, and 24 weeks etc.

Number of patients exposed to magrolimab for at least the following time periods: 1 day, 1 week, 4 weeks, 6 weeks, 8 weeks, 12 weeks, etc, in the original schedule of magrolimab administration before any repriming (Set 1) and number of patients entering maintenance period in Set 1 will be summarized.

The number of cycles patients are exposed to venetoclax or azacitidine will be summarized using descriptive statistics, and the number and percentage of patients who received at least 1, 2 …, 6, 9, 12, 15 cycles will be presented.

The number and percentage of patients who have infusion interruption, entire dose delayed or missed and the reasons will be summarized.

A by-subject listing of each study drug administration will be provided by treatment group, subject ID number (in ascending order) and visit (in chronological order).

4.2.1.2. Study drug: 7+3 Chemotherapy Regimen

The exposure to each of the chemotherapy agent will be summarized by the number of doses received using descriptive statistics. The number and percentage of patients who receive each distinct number of doses (5 doses, 7 doses, 14 doses, etc.) will be provided. The dose of cytarabine (HiDAC) used during consolidation cycles will be summarized.

The number and percentage of patients who received at least 1, 2 induction cycles and 1, 2, etc consolidation cycles will be presented.

4.2.2. Relative Dose Intensity

Relative dose intensity is the percentage of the total amount of study drug administered relative to the total amount of study drug expected to be administered during a subject's actual on-treatment period based on the study drug regimen.

For magrolimab:

The relative dose intensity is the percentage of the total amount of study drug administered relative to the total amount of study drug expected to be administered.

$$\text{Relative dose intensity (\%)} = \left(\frac{\text{Cumulative Dosages of Magrolimab Administered (in mg/kg)}}{\text{Magrolimab Dosage Expected to be Administered on Treatment(in mg/kg)}}\right) \text{x } 100$$

Cumulative dosage (mg/kg) administered for each subject is defined as the sum of dosages (mg/kg) of all infusions the subject received .

Magrolimab dosage expected to be administered on treatment (mg/kg) for each subject is defined as the total amount of magrolimab the subject was expected to receive during the subject's treatment period.

For venetoclax:

$$\text{Relative dose intensity (\%)} = \left(\frac{\text{Total Amount of Venetoclax Administered(mg)}}{\text{Venetoclax Expected to be Administered on Treatment (mg)}}\right) \text{x } 100$$

For azacitidine:

$$\text{Relative dose intensity (\%)} = \left(\frac{\text{Total Amount of Azacitidine Administered (mg/m2)}}{\text{Azacitidine Expected to be Administered on Treatment(mg/m2)}}\right) \text{x } 100$$

For each study drug, descriptive statistics for the relative dose intensity with the number and percentage of patients belonging to relative dose intensity categories (eg, < 75%, ≥ 75 to < 90%, ≥ 90%) will be provided by treatment group for the Safety Analysis Set.

For venetoclax, concomitant medications in Posaconazole/Other Strong CYP3A inhibitor/Moderate CYP3A inhibitor/P-gp inhibitor will be considered to reduce the amount of venetoclax expected to be administered.

4.3. Protocol Deviations

Protocol deviations occurring after patients entered the study are documented during routine monitoring. The number and percentage of patients with at least 1 important protocol deviations by deviation category (e.g., eligibility criteria, informed consent) will be summarized by treatment group for the ITT Analysis Set. A by-subject listing will be provided for those patients with important protocol deviation.

Patients who did not meet the eligibility criteria for study entry, but enrolled in the study will be presented regardless of whether they were exempted by the sponsor or not. A by-subject listing will be provided for those patients who did not meet at least 1 eligibility (inclusion or exclusion) criterion. The listing will present the eligibility criterion (or criteria if more than 1 deviation) that patients did not meet and related comments, if collected.

4.4. Assessment of COVID-19 Impact

This study was ongoing during the novel coronavirus disease (COVID-19) pandemic which has an impact on the study conduct. Some patients were unable to attend onsite visits due to shelter in place guidelines, site closures, or other reasons. This section describes how special situations due to COVID-19 will be handled in the analysis.

4.4.1. Study Drug Discontinuation Due to COVID-19

A summary of reasons for discontinuing study drug due to COVID-19 will be provided by treatment group and overall, similar to the summary described in the subject enrollment and disposition section (see Section 4.1).

A by-subject listing of reasons for study drug discontinuation due to COVID-19 will be provided if applicable.

4.4.2. Protocol Deviations Due to COVID-19

A by-subject listing will be provided for patients with protocol deviations related to COVID-19 if applicable.

4.4.3. Missed and Virtual Visits due to COVID-19

A by-subject listing of patients with missed or virtual visits due to COVID-19 will be provided if applicable.

4.4.4. Adverse Events Due to COVID-19

A by-subject listing of AEs of COVID-19 will be provided if applicable.

5. BASELINE CHARACTERISTICS

5.1. Demographics and Baseline Characteristics

Subject demographic variables (including age, age group [< 75 years, ≥ 75 years], sex, race/ ethnicity) and baseline characteristics (including body weight [in kg], height [in cm], body mass index [BMI; in kg/m^2], Body Surface Area [BSA; in m^2]) will be summarized by treatment group and overall using descriptive statistics for continuous variables and using number and percentage of patients for categorical variables. The summary of demographic data will be provided for the ITT Analysis Set.

A by-subject demographic listing, including the informed consent date, will be provided by treatment group and subject ID number.

5.2. Other Baseline Characteristics

Other baseline characteristics include but are not limited to biallelic 17p deletion/*TP53* mutational status, Eastern Cooperative Oncology Group (ECOG) performance status, and World Health Organization (WHO) AML classification, and investigators' reasons for appropriateness of non-intensive therapy. These baseline characteristics will be summarized by treatment group and overall using descriptive statistics for continuous variables and using number and percentage of patients for categorical variables. The summary of these baseline characteristics will be provided for the ITT Analysis Set. No formal statistical testing is planned.

A by-subject listing of other baseline characteristics will be provided.

5.3. Medical History

Medical history will be collected at screening for disease-specific and general conditions (ie, conditions not specific to the disease being studied).

General medical history data will not be coded, but will be listed only. A by-subject listing of general medical history will be provided by subject ID number in ascending order.

6. EFFICACY ANALYSES

6.1. Primary Efficacy Endpoint

6.1.1. Definition of Primary Efficacy Endpoint

The primary efficacy endpoint of this study is overall survival (OS) in the stratum of patients appropriate for non-intensive therapy. OS is defined as the interval from the date of randomization to the date of death from any cause. Patients whose deaths are not observed during the study will be censored at the last date that they were known to be alive.

The last known alive date for a subject will be determined by selecting the last available date across all datasets.

Every attempt will be made to ensure that complete death dates are recorded. In those rare instances where complete death dates are not recorded, the following algorithm will be used:

- If day is missing but the month and year are available, then the imputed date will be the first day of the month or the last known alive date + 1, whichever is later.
- If day and month are missing but year is available, then the imputed date will be 01Jan of that year or the last known alive date + 1, whichever is later.

6.1.2. Statistical Hypothesis for the Primary Efficacy Endpoint

The primary efficacy hypothesis to be tested is that there is no difference between magrolimab + azacitidine (experimental arm) and venetoclax + azacitidine (control arm) in OS for patients appropriate for non-intensive therapy. Using $S_E(t)$ and $S_C(t)$ to denote the OS distribution functions of the experimental arm and control arm, respectively, the statistical hypotheses to be tested in this study will be:

H_0: $S_E(t) = S_C(t)$ at all time points t

H_1: $S_E(t) > S_C(t)$ (experimental arm is superior to control arm in terms of OS for some $t > 0$)

6.1.3. Analysis of Primary Efficacy Endpoint

The primary analysis of OS will compare the OS distributions of two treatment groups in patients appropriate for non-intensive therapy using the stratified log-rank test, stratified by the stratification factors at randomization for the ITT Analysis Set. Medians, Q1, Q3 of the OS distributions, and the proportion of patients who are alive at 3, 6, 9, and 12 months from randomization will be estimated along with corresponding 95% CIs using the Kaplan-Meier method. Kaplan-Meier curves will be provided by treatment group.

In addition, the HR between the 2 treatment groups and its 95% CI will be estimated using the Cox proportional hazards regression model with Efron's method of tie handling, stratified by the stratification factors at randomization.

6.1.4. Follow-up Time

The follow-up time for OS is defined as the interval from date of randomization to the death date for patients who died during the study, or from the date of randomization to the earlier of the loss to follow-up or the last known alive date for patients who are alive while on study or loss to follow-up. The follow-up time will be summarized by treatment groups using descriptive statistics including median and range (minimum and maximum).

6.1.5. Sensitivity Analyses of the Primary Efficacy Endpoint

To assess the robustness of the primary OS results, the following sensitivity analyses will be performed:

Sensitivity Analyses (same definition of the endpoint, different analysis approach):

- OS will be analyzed using the unstratified log-rank test.

6.2. Secondary Efficacy Endpoints

6.2.1. Definition of Secondary Efficacy Endpoints

Overall Survival in All Patients: The OS is measured from the date of randomization to the date of death from any cause. Those whose deaths are not observed during the study will be censored at their last known alive date.

Event-Free Survival in All Patients: The EFS is defined as time from the date of randomization to the earliest date of the documented relapse from CR, treatment failure (defined as failure to achieve CR within 6 months of treatment with magrolimab + azacitidine or venetoclax + azacitidine, or up to 2 months of treatment with 7 + 3 chemotherapy), or death from any cause. Response assessments or death post SCT or new anti-AML therapies will be included in the analysis. The date of randomization will be assigned as the event date for patients with treatment failure.

Patients who are not observed to have one of the above specified events during the study will be censored at the date of their last response assessment with clear documentation of no relapse while on study. Patients will be censored at the date of randomization if no response assessment is performed after randomization and the patients did not die.

Table 6-1 summarizes the details of the EFS derivation algorithm.

Table 6-1. Censoring Rules for EFS

Scenario		Event/Censored	Event/Censored Date
Subject achieved CR* within 6 months from the randomization date (or 2 months of treatment with 7 + 3 chemotherapy)	Had relapse or death	Event (Relapse/death)	Relapse date or death date whichever occurs first
	No relapse or death	Censored	Last assessment date
Within 6 months (or 2 months of treatment with 7 + 3 chemotherapy), subject had at least one post-baseline assessment, but didn't achieve CR within that time	Had progression, death or new anti-AML therapies within the window	Event (Treatment Failure)	Randomization Date
	No progression, death or new anti-AML therapies within the window, and have been on study beyond the window	Event (Treatment Failure)	Randomization Date
	No progression, death or new anti-AML therapies within the window, and haven't been on study beyond the window	Censored	Randomization Date
Within 6 months (or 2 months of treatment with 7 + 3 chemotherapy), subject had no post-baseline response assessment	Had death or new anti-AML therapies within the window	Event (Treatment Failure)	Randomization Date
	No death or new anti-AML therapies within the window	Censored	Randomization Date

*CRs achieved before SCT or new anti-AML therapies.

When the date of initiation of a new anti-AML therapy other than the study treatment or the date of SCT is incomplete or missing, the following algorithm will be followed:

- If the day is missing but the month and year are available, then the imputed day will be the first day of the month or the day of last dose + 1 if the month and year of new anti-AML therapy/SCT and the month and year of last dose are the same.
- If day and month are missing but year is available, then the imputed day and month will be 01Jan, or the date of last dose + 1 if the year of new anti-AML therapy/SCT and the year of last dose are the same.

Rate of CR within 6 Months of Treatment in All Patients (2 months for patients receiving 7 + 3 chemotherapy): The CR rate is the proportion of patients who achieve a CR, including CR_{MRD-} and CR with positive or unknown minimal residual disease ($CR_{MRD+/unk}$) within 6 months of treatment with magrolimab + azacitidine or venetoclax + azacitidine, or within 2 months of treatment with 7 + 3 chemotherapy, as defined by investigators based on the ELN 2017 for AML with modifications (Protocol Appendix 6), while on study prior to initiation of any new anti-AML therapy or SCT.

Rate of CR_{MRD-} within 6 Months of Treatment in All Patients (2 months for patients receiving 7 + 3 chemotherapy): The CR_{MRD-} rate is the proportion of patients who achieve a CR_{MRD-} within 6 months of treatment with magrolimab + azacitidine or venetoclax + azacitidine, or within 2 months of treatment with 7 + 3 chemotherapy, as defined by investigators based on the ELN 2017 for AML with modifications (Protocol Appendix 6), while on study prior to initiation of any new anti-AML therapy or SCT.

Rate of CR+CRh within 6 Months of Treatment in All Patients (2 months for patients receiving 7 + 3 chemotherapy): The CR + CRh rate is the proportion of patients who achieve a CR (including CR_{MRD-} and $CR_{MRD+/unk}$) or CRh as defined by CR with partial platelet and absolute neutrophil count recovery (Protocol Appendix 6) within 6 months of treatment with magrolimab + azacitidine or venetoclax + azacitidine, or within 2 months of treatment with 7 + 3 chemotherapy while on study prior to initiation of any new anti-AML therapy or SCT.

Duration of CR: The DCR is measured from the time the assessment criteria are first met for CR (including CR_{MRD-} and $CR_{MRD+/unk}$) within 6 months of treatment with magrolimab + azacitidine or venetoclax + azacitidine, or within 2 months of treatment with 7 + 3 chemotherapy until the first date of AML relapse or death (including assessments post SCT). Those who are not observed to have relapsed disease or death while on study will be censored at the date of their last response assessment with no evidence of relapse during the study. If patients start taking new anti-AML therapies (excluding post-SCT maintenance therapy) before relapse, DCR will be censored at the last response assessment before the initiation of the new anti-AML therapies.

Duration of CR+CRh: The duration of CR+CRh is measured from the time the assessment criteria are first met for CR (including CR_{MRD-} and $CR_{MRD+/unk}$) or CRh within 6 months of treatment with magrolimab + azacitidine or venetoclax + azacitidine, or within 2 months of treatment with 7 + 3 chemotherapy until the first date of AML relapse or death (including assessments post SCT). Those who are not observed to have relapsed disease or death while on study will be censored at the date of their last response assessment with no evidence of relapse. If patients start taking new anti-AML therapies (excluding post-SCT maintenance therapy) before relapse, duration of CR+CRh will be censored at the last response assessment before the initiation of the new anti-AML therapies.

6.2.2. Analysis Methods for Secondary Efficacy Endpoints

Key secondary efficacy endpoints will be tested according to the order specified in Section 2.1.3, after the superiority for the primary efficacy endpoint is established.

6.2.2.1. Overall Survival in All Patients

Analyses of OS in all patients will be conducted in a similar manner as that of the primary efficacy endpoint OS in the stratum of patients appropriate for non-intensive therapy, as specified in Section 6.1.3. Sensitivity analyses of OS in all patients will be conducted similarly as specified in Section 6.1.5.

6.2.2.2. Event-Free Survival in All Patients

The distribution of EFS in all patients will be estimated for each treatment arm using Kaplan-Meier methodology and compared between treatment arms using the stratified log-rank test, stratified by the stratification factors at randomization for the ITT Analysis Set. Medians, Q1, Q3 of the EFS distributions, and the proportion of patients who are event-free at 3, 6, 9, and 12 months from randomization will be estimated along with corresponding 95% CIs using the Kaplan-Meier method. Kaplan-Meier curves will be provided by treatment group. The hazard ratio between treatment arms along with 95% CI will be estimated using the Cox proportional hazards regression model stratified by the stratification factors at randomization.

6.2.2.3. CR rate, CR_{MRD-} rate, CR+CRh rate and Durations of Remissions

The point estimate of the CR rate within 6 months (2 months for patients receiving 7+3 chemotherapy) and the corresponding 2-sided exact 95% CI based on the Clopper-Pearson method will be provided for each arm in the ITT Analysis Set. Patients, who are randomized but have no on-study response assessment or receive any new anti-AML therapy or SCT prior to achieving CR, will be considered as non-responders.

CR rates between the 2 treatment arms will be compared using the Cochran-Mantel-Haenszel test, stratified by the randomization stratification factors. Odds ratio comparing the 2 arms adjusted for the stratification factors will be presented along with 95% CI.

The CR_{MRD-} rate and CR+CRh rate will be evaluated in a similar manner as the CR rate.

For the time-to-event endpoints of DCR and duration of CR+CRh, analyses will be conducted based on the subsets on which the outcome measures are defined. Specifically, DCR will be based on patients who achieve CR, and duration of CR+CRh will be based on patients who achieve CR or CRh. Kaplan-Meier method will be used to estimate median duration with its 95% CI.

6.3. Estimands for Primary and Key Secondary Endpoints

Following the ICH E9 (R1) Addendum on Estimands and Sensitivity Analysis in Clinical Trials, a summary of the aforementioned primary and key secondary endpoints are presented in the estimand framework. Table 6-2 summarizes the attributes of estimands and estimators defined for main analyses and sensitivity analyses. The sensitivity analyses will not be included in the hierarchical testing planned in Section 2.1.3.

The **target population** of the estimand for the primary objective is AML *TP53* mutant patients appropriate for non-intensive therapy. For all the estimands of secondary objectives listed in the tables except for transfusion independence conversion, the **target population** attribute is all AML *TP53* mutant patients defined by the study inclusion and exclusion criteria. For transfusion independence conversion rates, the target population attribute is the AML *TP53* mutant patients defined by the inclusion and exclusion criteria with transfusion dependence at baseline.

Table 6-2. Estimands and Estimators of Main Analyses and Sensitivity Analyses for the Primary and Key Secondary Efficacy Endpoints

Treatments	Variable (Endpoint)	Intercurrent Events & Strategies	Population Level Summary	Estimators
magrolimab + azacitidine (experimental arm) vs. venetoclax + azacitidine (control arm), and with SCT/new anti-AML therapy as needed	OS (in patients appropriate for non-intensive therapy)	• Discontinuation of treatment: treatment policy • SCT, New anti-AML therapy: treatment policy	Kaplan-Meier estimates, hazard ratio	**Main Estimator:** Test the difference by a stratified logrank test; Estimate hazard ratio from a stratified Cox regression model. **Sensitivity Estimator:** Test the difference by a unstratified logrank test; Estimate hazard ratio from a unstratified Cox regression model.
magrolimab + azacitidine (experimental arm) vs. physician's choices of venetoclax + azacitidine or intensive therapy (control arm), and with SCT/new anti-AML therapy as needed	OS (in all patients)	• Discontinuation of treatment: treatment policy • SCT, New anti-AML therapy: treatment policy	Kaplan-Meier estimates, hazard ratio	**Main Estimator:** Test the difference by a stratified logrank test; Estimate hazard ratio from a stratified Cox regression model. **Sensitivity Estimator:** Test the difference by a unstratified logrank test; Estimate hazard ratio from a unstratified Cox regression model.
magrolimab + azacitidine vs. physician's choices of venetoclax + azacitidine or intensive therapy, and with SCT as needed	EFS	• Discontinuation of treatment: treatment policy • Death, Treatment failure: composite • SCT: treatment policy • New anti-AML therapy: treatment policy	Kaplan-Meier estimates, hazard ratio	**Main Estimator:** Test the difference by a stratified logrank test; Estimate hazard ratio from a stratified Cox regression model.

Treatments	Variable (Endpoint)	Intercurrent Events & Strategies	Population Level Summary	Estimators
magrolimab + azacitidine vs. physician's choices of venetoclax + azacitidine or intensive therapy	CR / CR_{MRD-} / CR+CRh	• Discontinuation of treatment: treatment policy • SCT, New anti-AML therapy: while-on-treatment	Odds ratio; CR rate/ CR_{MRD-} rate/ rate of CR+CRh while on study, prior to initiation of SCT or new anti-AML therapy	**Main Estimator:** Test the treatment effect in terms of odds ratio by a stratified Cochran-Mantel-Haenszel test; Estimate rate and CIs based on the Clopper-Pearson method.

CCI [redacted]

[redacted]

CCI

[redacted]

CCI [redacted]

6.5. Other Efficacy Related Analyses

6.5.1. Time to Complete Remission

Time to complete remission response (TCR) is defined as the interval from randomization to the first documentation of CR (CR_{MRD-} or $CR_{MRD+/unk}$) prior to initiation of new anti-AML therapy or SCT. TCR may be summarized using descriptive statistics by treatment group for patients achieving at least one of the CR as defined in the ITT Analysis Set.

6.5.2. Anti-AML Therapies

All post treatment anti-AML therapies will be provided in a by-subject listing sorted by subject ID number, treatment group, and administration date in chronological order.

6.5.3. RBC and Platelet Transfusions

A by-subject listing for RBC and platelet transfusions required throughout the study will be provided by subject ID and treatment group in chronological order. Date of transfusion, transfusion type, and the number of units transfused will be presented.

6.6. Patient-Reported Outcome

6.6.1. Definition of Patient-Reported Outcome Data

Four patient-reported outcome (PRO) instruments will be administered in this study: the EORTC- QLQ-C30, the EQ-5D-5L, the PGIS, and the PGIC.

The EORTC QLQ-C30 is a 30-item PRO instrument that assesses cancer-related symptoms and impacts. The instrument is separated into 5 functional scales (physical functioning, role functioning, emotional functioning, cognitive functioning, and social functioning), 1 global health status scale, 3 multi-item symptom scales (fatigue, nausea and vomiting, and pain) and 6 single-item symptom scales (dyspnea, insomnia, loss of appetite, constipation, diarrhea, and financial difficulties). Subjects rate items on a four-point scale, with 1 as "not at all" and 4 as "very much", except that the GHS/QoL which utilizes a 7-point scale. Items 1 to 5 has an unspecified recall period, and the remaining items have a recall period “in the past week”.

The EQ-5D-5L is an instrument for use as a measure of health outcome and consists of 2 sections: the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS). The questionnaire is provided in the protocol Appendix 8.

The EQ-5D descriptive system comprises 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The patient is asked to indicate his/her health state by ticking the box next to the most appropriate statement in each of the 5 dimensions. This decision results in a 1-digit number that expresses the level selected for that dimension. The digits for the 5 dimensions can be combined into a 5-digit number that describes the patient’s health state.

The EQ VAS records the patient’s self-rated health on a vertical VAS, where the endpoints are labeled “the best health you can imagine” and “the worst health you can imagine.” The EQ VAS can be used as a quantitative measure of health outcome that reflects the patient’s own judgment.

The PGIS and PGIC assessments are both single-item assessments used to demonstrate sensitivity and meaningful change thresholds and bolster the validity of selected PRO assessments for health-related quality of life and the physical function. The questionnaires are provided in the protocol Appendix 9.

6.6.2. Analysis of Patient-Reported Outcome Data

Because the study was terminated early due to futility, analyses of the PRO endpoints are not planned for the final CSR. Previously planned PRO analyses are documented in the following paragraphs.

CCI [redacted]

Raw scores of domain scales/items from the EORTC QLQ-C30 will be transformed to 0-100 before analysis according to the current EORTC QLQ-C30 Scoring Manual (3rd Edition). TTD on the GHS/QoL scale and TTD on the physical functioning scale will be respectively analyzed using the Kaplan-Meier method on the ITT Analysis Set. The log-rank test stratified by randomization stratification factors will be conducted for the TTD comparison between treatment arms, and the HR estimated using a Cox proportional hazard regression model stratified by randomization stratification factors will be provided.

The EQ-5D-5L questionnaire data will be scored, processed, and standardized according to the user manual. The EQ-5D-5L status will be converted into a single preference-weighted health utility index score by applying US weights, unless otherwise specified.

Descriptive statistics will be calculated for all the EORTC QLQ-C30 symptom and functioning scales and single items the EQ-5D-5L utility score, the EQ-5D VAS score, and PGIS/PGIC response score at scheduled assessments. The mean and change from baseline to each subsequent assessment will be summarized by treatment group. Changes from baseline in HRQoL as measured by mean change from baseline scores in scales/items of the EORTC QLQ-C30, EQ VAS score, and EQ-5D-5L utility score will be analyzed.

Proportion of patients who report each response category on the PGIC and PGIS at scheduled time-point will be summarized by treatment group. The mean and change from baseline on the PGIS to each subsequent assessment may be summarized.

7. SAFETY ANALYSES

7.1. Adverse Events and Deaths

7.1.1. Adverse Event Dictionary

Clinical and laboratory adverse events (AEs) will be coded using MedDRA v26.1. System organ class (SOC), high-level group term (HLGT), high-level term (HLT), preferred term (PT), and lower-level term (LLT) will be provided in the AE dataset.

7.1.2. Adverse Event Severity

Adverse events are graded by the investigator as Grade 1, 2, 3, 4, or 5 according to Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. The severity grade of events for which the investigator did not record severity will be categorized as "missing" for tabular summaries and data listings. The missing category will be listed last in summary presentation.

7.1.3. Relationship of Adverse Events to Study Drug

Related AEs are those for which the investigator selected "Related" for a study drug on the AE CRF to the question of "Related to Study Treatment." Relatedness will always default to the investigator's choice, not that of the medical monitor. Events for which the investigator did not record relationship to study drug will be considered related to study drug for summary purposes. However, by-subject data listings will show the relationship as missing.

7.1.4. Serious Adverse Events

Serious adverse events (SAEs) will be identified and reported as SAEs if the AEs met the definitions of SAEs that were specified in the study protocol. SAEs captured and stored in the clinical database will be reconciled with the SAE database from the Gilead Global Patient Safety before data finalization.

7.1.5. Treatment-Emergent Adverse Events

7.1.5.1. Definition of Treatment-Emergent Adverse Events

Treatment-emergent adverse events (TEAEs) are defined as any AE that begins on or after the date of first dose of study treatment up to the date of last dose of study treatment plus 70 days or the day before initiation of new anti-AML therapy including SCT, whichever occurs first. If the AE onset date is on or before the last dose date, the AE is considered as TEAE regardless of the start of new anti-AML therapy.

7.1.5.2. Incomplete Dates

If the onset date of the AE is incomplete and the AE stop date is not prior to the first dosing date of study drug, then the month and year (or year alone if month is not recorded) of onset determine whether an AE is treatment emergent. The event is considered treatment emergent if both of the following 2 criteria are met:

- The AE onset is the same as or after the month and year (or year) of the first dosing date of study drug, and
- The AE onset date is the same as or before the month and year (or year) of the date corresponding to the cutoff date of TEAE period, which is defined as the 70 days after the study drug last dose date or the day before initiation of any new anti-AML therapy including SCT, whichever occurs first.

An AE with completely missing onset and stop dates, or with the onset date missing and a stop date later than the first dosing date of study drug, will be considered to be treatment emergent. In addition, an AE with the onset date missing and incomplete stop date with the same or later month and year (or year alone if month is not recorded) as the first dosing date of study drug will be considered treatment emergent.

In case when the AE onset date is incomplete and needs to be imputed, the following algorithm will be followed:

- If the day is missing but the month and year are available, then the imputed day will be the first dosing date if they have the same month and year, or the first day of the month otherwise.
- If the day and month are missing but year is available, then the imputed day and month will be the first dosing date if they have the same year, or 01Jan otherwise.

7.1.6. Summaries of Adverse Events and Deaths

Treatment-emergent AEs will be summarized based on the Safety Analysis Set.

7.1.6.1. Summaries of AE incidence in Combined Severity Grade Subsets

A brief, high-level summary of the number and percentage of patients who experienced at least 1 TEAE in the categories described below will be provided by treatment group. All deaths observed in the study will also be included in this summary.

The number and percentage of patients who experienced at least 1 TEAE will be provided and summarized by SOC, PT, and treatment group.

For the AE categories described below, summaries will be provided by SOC, PT, maximum severity (as applicable), and treatment group:

- TEAEs
- TEAEs with Grade 3 or higher
- Treatment-related TEAEs for each study drug
- TE SAEs
- Treatment-related TE SAEs for each study drug
- TEAEs leading to discontinuation of each study drug
- TEAEs leading to death
- TEAEs leading to dose interruption of study drug (magrolimab, azacitidine, venetoclax)
- TEAEs leading to dose reduction of study drug (magrolimab, azacitidine, venetoclax)

Multiple events will be counted only once per subject in each summary. Adverse events will be summarized and listed first in alphabetic order of SOC and then by PT in descending order of total frequency within each SOC. For summaries by severity, the most severe severity will be used for those AEs that occurred more than once in a given subject during the study.

In addition to the above summary tables, all TEAEs, TEAEs of Grade 3 or higher, TE SAEs and Treatment-related TEAEs and Treatment-related TE SAEs will be summarized by PT only in descending order of total frequency.

In addition, data listings will be provided for the following:

- All AEs, indicating whether the event is treatment emergent
- All SAEs
- All Deaths
- All AEs leading to death
- All AEs with severity of Grade 3 or higher
- All AEs leading to discontinuation of magrolimab
- AEs leading to dose interruption of magrolimab

A summary (number and percentage of patients) of deaths will be provided by treatment group. Summary will include the following categories:

- All deaths
- Deaths within 30 days of the first dosing of study drug
- Deaths within 60 days of the first dosing of study drug
- Deaths within 30 days of the last dosing of study drug
- Deaths beyond 30 days of the last dosing of study drug
- Deaths within 70 days of the last dosing of study drug
- Deaths beyond 70 days of the last dosing of study drug

7.1.7. Additional Analysis of Adverse Events

7.1.7.1. Treatment-Emergent Adverse Events (TEAEs) of Special Interest

Number and percentage of patients with the following AEs of special interest will be summarized by PT:

- Anaemia (MedDRA Search Term (MST) - Anemia Extravascular Transient Hemolysis)
- Infusion-Related Reaction (IRR) (Standardised MedDRA Queries (SMQ)-Hypersensitivity Narrow Terms) + within one day of latest infusion of any study drug
- Severe Neutropenia (PT - Neutrophil Count Decreased, Neutropenia and Febrile Neutropenia with Grade 3 or Higher)
- Serious Infections (SOC - Infections and infestations with Serious AE)
- Transfusion reactions due to magrolimab interference with RBC typing (Gilead's MST)
- Thromboembolic Events (SMQ- Embolic and Thrombotic Events Broad Terms)
- Pneumonitis (SMQ- Interstitial Lung Disease Broad Terms)

Number and percentage of patients with the following AEs of special interest will also be summarized by AE onset time within 2 weeks, >2weeks - 2 months, >2 months to 6 months, >6 months to 12 months, and >12 months of first dosing of any study drug:

- Anaemia
- IRR
- Severe Neutropenia

- Serious Infections
- Transfusion reactions due to magrolimab interference with RBC typing
- Thromboembolic Events
- Pneumonitis

A high-level summary of the number and percentage of patients who experienced at least 1 AE of special interest as defined above will be provided by treatment group.

7.1.7.2. Other Important Safety Topics

Number and percentage of patients with the following AEs of important safety topics will be summarized by PT:

- Immune-Mediated Events (SMQ-Immune-mediate and autoimmune disorder Narrow Terms)
- Hemorrhages (SMQ - Haemorrhages Broad Terms)

Number and percentage of patients with the AEs of important safety topics will also be summarized by first AE onset time within 2 weeks, >2 weeks to 2 months, >2 months to 6 months, >6 months to 12 months, and >12 months of first dosing of any study drug.

A high-level summary of the number and percentage of patients who experienced at least 1 AE of important safety topics as defined above will be provided by treatment group.

7.1.7.3. Regrouped AE Terms

For the regrouped AE terms described below, summaries will be provided by treatment group:

- Regrouped Anaemia and Haemoglobin Decreased
- Regrouped Neutropenia and Neutrophil Count Decreased
- Regrouped Thrombocytopenia and Platelet Count Decreased

7.2. Laboratory Evaluations

Laboratory data collected during the study will be analyzed and summarized using both quantitative and qualitative methods. Summaries of laboratory data will be provided for the Safety Analysis Set and will include data collected up to the last dose of study drug plus 70 days or the day before initiation of new anti-AML therapy including SCT, whichever occurs first. If the laboratory data collection date is on or before the last dose date, the laboratory data is included regardless of the start of new anti-AML therapy. The analysis will be based on values reported in conventional units. When values are below the LOQ, they will be listed as such, and the closest imputed value will be used for the purpose of calculating summary statistics as specified in Section 3.7.

A by-subject listing for laboratory test results will be provided by treatment group, subject ID and visit in chronological order for hematology and serum chemistry separately. Values falling outside of the relevant reference range and/or having a severity grade of 1 or higher on the CTCAE severity grade will be flagged in the data listings, as appropriate.

No formal statistical testing is planned.

7.2.1. Summaries of Numeric Laboratory Results

Descriptive statistics will be provided by treatment group for hematology and serum chemistry laboratory tests specified in the study protocol as follows:

- Baseline values
- Postbaseline maximum and minimum values
- Change and percentage change from baseline to postbaseline maximum and minimum value

A baseline laboratory value will be defined as the last measurement obtained on or prior to the date/time of first dose of any study drug. Change from baseline to a postbaseline visit will be defined as the postbaseline value minus the baseline value. The mean, median, Q1, Q3, minimum, and maximum values will be displayed to the reported number of digits; StD values will be displayed to the reported number of digits plus 1.

Median (Q1, Q3) of the observed values will be plotted using a line plot by treatment group and visit for the laboratory tests including but not limited to hemoglobin, platelet, and absolute neutrophil counts.

In the case of multiple values associated with a visit, data will be selected for analysis as described in Section 3.8.3.

7.2.2. Graded Laboratory Values

The CTCAE Version 5.0 will be used to assign toxicity grades (0 to 4) to laboratory results for analysis. Grade 0 includes all values that do not meet the criteria for an abnormality of at least Grade 1. For laboratory tests with criteria for both increased and decreased levels, analyses for each direction (ie, increased, decreased) will be presented separately.

7.2.2.1. Treatment-Emergent Laboratory Abnormalities

Treatment-emergent laboratory abnormalities are defined as values that increase at least 1 toxicity grade from baseline at any postbaseline time point ,up to and including the date of last dose of study treatment plus 70 days or the day before initiation of any new anti-AML therapy including SCT, whichever occurs first. If the relevant baseline laboratory value is missing, any abnormality of at least Grade 1 observed within the time frame specified above will be considered treatment emergent.

7.2.2.2. Summaries of Laboratory Abnormalities

Laboratory data that are categorical will be summarized using the number and percentage of patients in the study with the given response at baseline and each scheduled postbaseline time point.

The following summaries (number and percentage of patients) for treatment-emergent laboratory abnormalities will be provided by laboratory test and treatment group; patients will be categorized according to the most severe postbaseline abnormality grade for a given laboratory test:

- Graded TE laboratory abnormalities
- TE Grade 3 or 4 laboratory abnormalities

For all summaries of laboratory abnormalities, the denominator is the number of patients with nonmissing postbaseline values up to 70 days after the last dosing date or the day before initiation of new anti-AML therapy including SCT, whichever occurs first.

A by-subject listing of treatment-emergent Grade 3 or 4 laboratory abnormalities will be provided by subject ID number and visit in chronological order. This listing will include all test results that were collected throughout the study for the lab test of interest, with all applicable severity grades displayed.

7.2.3. Liver-related Laboratory Evaluations

Liver-related abnormalities after initial study drug dosing will be examined and summarized using the number and percentage of patients who were reported to have the following laboratory test values for postbaseline measurements:

- Aspartate aminotransferase (AST): > 3 times of the upper limit of reference range (ULN)
- Alanine aminotransferase (ALT): > 3 x ULN
- AST or ALT: > 3 x ULN
- Total bilirubin: > 2 x ULN
- AST or ALT > 3 x ULN and total bilirubin > 2 x ULN
- AST or ALT > 3 x ULN and total bilirubin > 2 x ULN and alkaline phosphatase (ALP) < 2 x ULN

The summary will include data from all postbaseline visits up to 70 days after the last dose of study drug, or the day before initiation of any new anti-AML therapy including SCT, whichever occurs first. For individual laboratory tests, patients will be counted once based on the most

severe postbaseline values. For the composite endpoints of AST or ALT, and total bilirubin, patients will be counted once when the criteria are met at the same postbaseline visit date. The denominator is the number of patients in the Safety Analysis Set who have nonmissing postbaseline values of all relevant tests at the same postbaseline visit date.

A listing of patients who met at least 1 of the above criteria will be provided.

7.3. Body Weight and Vital Signs

No summary or listing of body weight, BMI or vital signs will be provided to align with the planned scope of the study synoptic CSR.

7.4. Prior and Concomitant Medications

Medications collected at screening and during the study will be coded using the current version of the World Health Organization (WHO) Drug dictionary.

7.4.1. Prior Medications

Prior medications are defined as any medications taken before a subject takes the first study drug. For the purposes of analysis, any medication with a start date prior to the first dosing date of study drug will be categorized as the prior medication regardless of when the stop date is. If a partial start date is entered, the medication will be considered prior unless the month and year (if day is missing) or year (if day and month are missing) of the start date are after the first dosing date. Medications with a completely missing start date will be included in the prior medication summary, unless otherwise specified.

7.4.2. Concomitant Medications

Concomitant medications are defined as medications taken while a subject took study drug. For the purposes of analysis, any medications with a start date prior to or on the first dosing date of study drug and continued to be taken after the first dosing date, or started after the first dosing date but prior to or on 70 days after the last dosing date of study drug will be considered concomitant medications. Medications started and stopped on the same day as the first dosing date or 70 days after the last dosing date of study drug will also be considered concomitant. Medications with a stop date prior to the date of first dosing date of study drug or a start date after the last dosing date of study drug plus 70 days will be excluded from the concomitant medication summary. If a partial stop date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) prior to the date of first study drug administration will be excluded from the concomitant medication summary. If a partial start date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) after the study drug stop date plus 70 days will be excluded from the concomitant medication summary. Medications with completely missing start and stop dates will be included in the concomitant medication summary, unless otherwise specified.

All prior and concomitant medications (other than per-protocol study drugs) will be provided in a by-subject listing sorted by subject ID number and administration date in chronological order. Analysis will be based on the ITT Analysis Set. No formal statistical testing is planned.

7.5. Electrocardiogram Results

A standard 12-lead electrocardiogram (ECG) will be performed using local standard procedures at screening for all patients and at subsequent visits for patients undergoing treatment with 7+3 intensive therapy, as specified in Appendix 2 of the protocol. Electrocardiogram (ECG) analysis results are intended to identify meaningful changes in the QT interval. Because the study was terminated early due to futility, no ECG analysis is planned for the final CSR.

7.6. Other Safety Measures

A by-subject listing of pregnancy test report will be provided by subject ID number in ascending order.

7.7. Changes from Protocol-Specified Safety Analyses

There are no deviations from the protocol-specified safety analyses.

8. PHARMACOKINETIC (PK) AND IMMUNOGENECITY ANALYSES

8.1. PK Sample Collection

Blood samples for evaluating magrolimab serum concentrations will be collected as described in Protocol Appendix 2.

8.2. PK Analyses

The magrolimab PK concentration will be summarized for the PK Analysis Set. Individual subject's concentration data for magrolimab will be listed based on the sampling time point. Magrolimab PK data will be summarized using descriptive statistics. Summary statistics (n, mean, SD, coefficient of variation [%CV], median, min, max, Q1, and Q3) will be presented for magrolimab serum concentration data at time point.

The sample size (number of patients) at each time point will be based on the number of patients with nonmissing concentration data at that time point. Missing concentration values will be reported as is in data listings. The number of patients with concentration BLQ will be presented for each time point.

Sparse PK concentration values that are BLQ will be presented as "BLQ" in the concentration data listing. Values that are BLQ will be treated as 0 at predose and postdose time points for summary purposes.

At predose, if all concentration values are BLQ, then the mean, and order statistics (minimum, Q1, median, Q3, and maximum) will be displayed as 0 and the rest of the summary statistics (ie, SD and CV) will be missing. If any values are non-BLQ, then the number of samples, order statistics, and all summary statistics will be displayed.

At any given postdose time point, if more than one-third of the patients have a concentration value of BLQ , then only the number of samples and order statistics will be displayed; otherwise, order statistics and summary statistics will be displayed.

The following conventions will be used for the presentation of order statistics for postdose time points:

- If at least 1 subject has a concentration value of BLQ for the time point, the minimum value will be displayed as "BLQ."
- If more than 25% of the patients have a concentration data value of BLQ for a given time point, the minimum and Q1 values will be displayed as "BLQ."
- If more than 50% of the patients have a concentration data value of BLQ for a given time point, the minimum, Q1, and median values will be displayed as "BLQ."

- If more than 75% of the patients have a concentration data value of BLQ for a given time point, the minimum, Q1, median, and Q3 values will be displayed as "BLQ."

- If all patients have concentration data values of BLQ for a given time point, all order statistics (minimum, Q1, median, Q3, and maximum) will be displayed as "BLQ."

Due to the sparse nature of PK collection, PK parameters will not be calculated.

8.3. Immunogenicity Analysis

The rate and magnitude of anti-drug antibody (ADA) prevalence, incidence, persistence, and transience will be summarized for the Immunogenicity Analysis Set. Neutralizing antibody occurrence rate will also be summarized.

ADA Prevalence: the proportion of patients who had at least one positive ADA sample (baseline or post-baseline) based on the Immunogenicity Analysis Set.

Treatment-Induced ADA Rate: the proportion of patients who had negative baseline ADA sample and at least one positive post-treatment ADA sample based on patients who had both non-missing baseline and at least one post-treatment ADA result reported (i.e. ADA Incidence Analysis Set).

Treatment-Boosted ADA Rate: the proportion of patients who had positive baseline ADA sample and at least one positive post-treatment ADA sample and the (max titer of the post-treatment ADA) / (titer of baseline ADA) >= 4 based on the ADA Incidence Analysis Set.

ADA Incidence (treatment-emergent ADA): the proportion of patients who had treatment-induced or treatment-boosted ADA based on patients who had at least one non-missing baseline ADA sample and at least one post-treatment ADA result reported in Immunogenicity Analysis Set.

Persistent ADA is defined as:

a) Treatment-Induced ADA detected at two or more sampling time points during the treatment (including follow-up period if any), where the first and last ADA-positive sample (irrespective of any negative samples in between) are separated by a period of 16 weeks or longer.

or

b) Treatment-Induced ADA detected in the last sampling time point of the treatment study period.

ADA Persistence Rate: the proportion of patients who had persistent ADA based on the ADA Incidence Analysis Set.

Transient ADA is defined as:

Treatment-Induced ADA that does not meet the definition of persistent ADA. The proportion of patients who had transient ADA is based on the patients evaluable for ADA incidence.

Neutralizing antibody (NAb) Incidence: the proportion of patients who had at least one positive neutralizing antibody result reported based on the treatment-emergent ADA (treatment-induced or treatment-boosted ADA) among the patients evaluable for ADA incidence.

Titer summaries may also be generated, if relevant. CCI [redacted]

9. PHARMACODYNAMIC ANALYSES

CCI [redacted]

10. REFERENCES

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Lan KKG, Hu P, Proschan M. A Conditional Power Approach to the Evaluation of Predictive Power. Statistics in Biopharmaceutical Research 2012;1 (2):131-6.

Sallman DA, Asch A, Al-Malki M, Lee D, Garcia-Manero G, Donnellan W, et al. Tolerability and Efficacy of the First-in-Class Anti-CD47 Antibody Magrolimab Combined With Azacitidine in MDS and AML Patients: Phase 1b Results [Presentation]. American Society of Clinical Oncology (ASCO) Annual Meeting Virtual; 2020.

11. SOFTWARE

SAS® Software Version 9.4. SAS Institute Inc., Cary, NC, USA.

12. SAP REVISION

Revision Date (DD MMM YYYY)	Section	Summary of Revision	Reason for Revision

13. APPENDICES

Appendix 1. Schedule of Assessments

Appendix Table 1. Schedule of Assessments – Screening[a]

	Study
Assessment	**Day −30 to −1**
Bone marrow aspirate for central assessment of *TP53* mutation status[b]	X
Informed consent[a]	X
Demographics	X
Medical and cancer history	X
Serum pregnancy test[c]	X
CBC with differential, platelets, reticulocytes, blasts	X
Serum or plasma chemistry	X
PT, INR, and aPTT (or PTT)	X
Blood phenotyping or genotyping,[f] type, and screen (ABO/Rh), DAT	X
Urinalysis	X
Peripheral blood for MRD assessment[d]	X
Bone marrow biopsy and aspirate for blast evaluation, correlative studies, cytogenetics, and MRD assessment[b,e]	X
Peripheral blood smear (for blasts)[e]	X
ECOG performance status	X
Vital signs, height, and weight	X
Complete physical examination	X
HBV, HCV, and HIV	X
12-lead ECG (single)	X
Echocardiogram or MUGA (for patients appropriate for intensive therapy)	X
Adverse events related to protocol-mandated procedures	X
Prior and concomitant medications	X
Eligibility criteria	X
Randomization [a]	X

ABO = any of the 4 blood groups A, B, AB, and O comprising the ABO system; aPTT = activated partial thromboplastin time; CBC = complete blood count; DAT = direct antiglobulin test; ECG = electrocardiogram; ECOG = Eastern Cooperative Oncology Group; FSH = follicle-stimulating hormone; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; MRD = minimal residual disease; MUGA = multigated acquisition (scan); PT/INR = prothrombin time/international normalized ratio; PTT = partial thromboplastin time; RBC = red blood cells; Rh = rhesus factor

a Screening must be completed before randomization. Randomization must occur within 30 days of signing informed consent. The first dose of study treatment must be given within 72 hours after randomization.

b Bone marrow biopsy and aspirate for blast evaluation, correlative studies, cytogenetics and to assess *TP53* mutational status may take place as a prescreening assessment and will require an additional consent form. In that case, the MRD assessment will not be required.

c Screening pregnancy test may be used as the Cycle 1 Day 1 test if performed within 72 hours prior to first dose; additional guidance is provided in Protocol Amendment 5 Section 6.4.1. FSH test is required for female patients who are < 54 years old who are not on hormonal contraception and who have stopped menstruating for ≥ 12 months but do not have documentation of ovarian hormonal failure.

d Peripheral blood sample for MRD assessment must be collected prior to the first dose of study treatment at the latest.

e A trephine (biopsy) is to be collected for baseline. This procedure must be performed prior to the first dose of study treatment at the latest. An aspirate sample will be collected for blast evaluation, MRD assessment, correlative studies, and biobanking. Bone marrow aspirate samples are to be obtained at the time of bone marrow (trephine) biopsy. Conventional cytogenetics to be tested per institutional standards. Peripheral blood smear for blasts are to be collected along with bone marrow aspirate/biopsy.

f ABO/Rh type, antibody screen, DAT, and extended RBC phenotyping (including minor antigens such as CcDEe, Cw, MNSs, Kk, FyaFyb, and JkaJkb) must be performed for each patient. RBC genotyping instead of extended RBC phenotyping is acceptable for any patient. RBC genotyping (instead of an extended RBC phenotyping) must be performed if a patient received any RBC or whole blood transfusion within the previous 3 months (unless the laboratory has availability for special techniques for performing phenotyping for patients with a recent transfusion). Results must be available before the first dose of magrolimab.

Appendix Table 2. Schedule of Assessments - Treatment Period for Azacitidine (Experimental Arm) and Venetoclax + Azacitidine Regimens

	Cycle (28-day cycles)																																
	Cycle 1													Cycle 2												Cycle 3+								
Visit Window	None		± 3 Days											± 3 Days												± 3 Days								
Cycle Day	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**11**	**15**	**22**	**28**	**Twice Weekly Until Count Recovery (Max = 14 Days)[a]**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**15**	**22**	**28**	**Twice Weekly Until Count Recovery (Max = 14 Days)[a]**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**15**	**28**	**Twice Weekly Until Count Recovery (Max = 14 Days)[a]**
PRO Assessment[b]	X													X												X									
Serum or Urine Pregnancy Test[c]	X													X												X									
CBC with Differential, Platelets, Reticulocytes, Blasts[d,e]	X	X		X				X	X	X	X	X	X	X							X	X	X	X	X	X							X	X	X
Haptoglobin and LDH[d]	X	X		X				X						X																					
Serum or Plasma Chemistry[d]	X[f]	X[f]	X[f]	X[f]				X		X	X			X								X				X							X		
Peripheral Blood Smear (for General Morphology)[d,g]	X	X							X																										
Peripheral Blood Smear (for Blasts)[h]												X												X										C4D28, C6D28 then Q3C	
Buccal Swab[i]	X																																		

	Cycle (28-day cycles)																																		
	Cycle 1													Cycle 2												Cycle 3+										
Visit Window	**None**		**± 3 Days**											**± 3 Days**												**± 3 Days**										
Cycle Day	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**11**	**15**	**22**	**28**	**Twice Weekly Until Count Recovery (Max = 14 Days)[a]**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**15**	**22**	**28**	**Twice Weekly Until Count Recovery (Max = 14 Days)[a]**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**15**	**28**	**Twice Weekly Until Count Recovery (Max = 14 Days)[a]**
Peripheral Blood Sample for Correlative Studies[j]	X							X				X		X[k]										X										C6D28	
Peripheral Blood Sample for MRD Assessment[h]												X												X										C4D28, C6D28 then Q3C	
Bone Marrow Aspirate for Cytogenetics, MRD Monitoring and Response Assessment[h,l,m]												X												X										C4D28, C6D28 then Q3C	
Bone Marrow Aspirate and Biopsy for Correlative Studies[h]																								X										C6D28	
Vital Signs[n]	X	X						X	X	X	X			X							X	X	X			X							X			
Weight[n]	X													X												X										
Symptom-directed Physical Examination[d]	X							X		X				X												X										

	Cycle (28-day cycles)																																
	Cycle 1													Cycle 2												Cycle 3+								
Visit Window	None		± 3 Days											± 3 Days												± 3 Days								
Cycle Day	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**11**	**15**	**22**	**28**	**Twice Weekly Until Count Recovery (Max = 14 Days)[a]**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**15**	**22**	**28**	**Twice Weekly Until Count Recovery (Max = 14 Days)[a]**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**15**	**28**	**Twice Weekly Until Count Recovery (Max = 14 Days)[a]**
Adverse Events, Concomitant Medications (Including Blood Transfusions)[o]	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	
Study Treatment Dispensing																																			
Venetoclax[p]	X													X												X									
Study Treatment Administration																																			
Azacitidine[q]	X	X	X	X	X	X	X							X	X	X	X	X	X	X						X	X	X	X	X	X	X			
Venetoclax[p,r]	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	

C = cycle; CBC = complete blood count; D = day; EOT = end of treatment; EORTC QLQ- European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire -Core Questionnaire; EQ-5D-5L = 5-level EuroQol 5 dimensions; LDH = lactate dehydrogenase; MRD = minimal residual disease; PGIC = Patient Global Impression of Change; PGIS = Patient Global Impression of Severity; PRO = patient-reported outcome; Q3C = every 3 cycles; WBC = white blood cell

a If the patient is cytopenic at Day 28, CBC is to be monitored at least twice per week for 2 weeks or until optimal count recovery is reached (whichever comes first). The best CBC result within the ± 2-week window is to be used for the response assessment, with the date of response being the date of the bone marrow assessment. Complete blood count need not be repeated if the prior CBC (including prior Day 28 CBC) is within 3 days of Day 1.

b Four PRO instruments will be administered in this study: the EORTC QLQ-C30 questionnaire, the EQ-5D-5L, the PGIS, and the PGIC. The patient should complete these questionnaires before any other study procedures at required visits. EORTC QLQ-C30 and EQ-5D-5L questionnaires should be performed prior to PGIS/PGIC. PGIC is not required at Cycle 1 Day 1.

c Screening pregnancy test may be used if performed within 72 hours of first dose; pregnancy tests will be conducted on Day 1 of every cycle; additional guidance is provided in Protocol Amendment 5 Section 6.4.1.

d Pretreatment assessments for the initial dose (Cycle 1 Day 1) may be collected up to 72 hours before administration of any study treatment except for CBC, which must be performed within 24 hours prior to magrolimab dosing. Thereafter, pretreatment assessments are to be collected within 24 hours prior to any intravenous or subcutaneous study drugs during the first 2 weeks and within 72 hours prior to any intravenous or subcutaneous study drugs thereafter.

e Additional samples for CBC may be collected outside of the protocol-specified time points to ensure a WBC level $\leq 20 \times 10^3/\mu L$ prior to each magrolimab dose during Cycle 1.

f To monitor the risk of tumor lysis syndrome during venetoclax ramp-up, blood chemistry is to be collected predose and 6 to 8 hours postdose of venetoclax administration on Cycle 1 Day 1, Cycle 1 Day 2, and Cycle 1 Day 3. Blood chemistry on Cycle 1 Day 4 is to be collected 24 hours after the dose of venetoclax given on Cycle 1 Day 3.
g Peripheral blood smears will be collected at predose and assessed locally.
h Day 28 assessments can be done on Day 1 of the next cycle if there is no foreseen delay of more than 7 days. Bone marrow response information from Day 28 may be required to decide start of the next cycle per dosing modification guidelines in the protocol (Protocol Amendment 5 Section 5.10, and Table 8, Table 9, and Table 11). Collection of bone marrow aspirate and biopsy for correlative studies will be allowed within 7 days (rather than a 3-day window).
i Single sample will be collected on Day 1 or at any time during the study.
j Samples will be collected predose within 12 hours prior to study treatment administration.
k Peripheral blood samples for correlative studies do not need to be repeated at D1, if performed in the past 7 days. Collection of peripheral blood for correlative studies will be allowed within 7 days (rather than a 3-day window).
l Conventional cytogenetics to be tested per institutional standards.
m An aspirate sample will be collected for response assessment and MRD assessment. Response assessments may be adjusted by up to 1 week prior to Cycle 1 Day 28, and Cycle 2 Day 28. After Cycle 2 Day 28, the window is up to 14 days ± from Day 28. Bone marrow results are to be reviewed as required for determining schedule modifications.
n Vital signs will be assessed prior to infusion/injection of each study treatment on the days marked in the table. Weight will be assessed on Day 1 of each cycle. Details are provided in Protocol Amendment 5 Section 6.4.5.
o Collected at all regularly scheduled visits.
p Venetoclax will be dispensed to the patient on Day 1 of each treatment cycle.
q Azacitidine administration should be completed at least 1 hour before magrolimab administration on days when both drugs are administered. Azacitidine may be administered on an alternative schedule such as Days 1 to 5, Day 8, and Day 9 of a 28-day cycle for flexibility and convenience as long as the 7 doses of azacitidine of the cycle are administered within 9 consecutive days.
r Venetoclax is administered daily. Please refer to Protocol Amendment 5 Section 5.4.

Appendix Table 3. Magrolimab Administration and Associated Assessment Schedule-Treatment Period

Visit Window (Days)	None[a]			± 3[a]				
Day	**1**	**2**	**4**	**8**	**11**	**15**	**Weekly × 5**	**Every 2 Weeks**
Vital signs[b]	X		X	X	X	X	X	X
Hemoglobin[c]	Pre and post dose		Pre and post dose					
PK	Within 72 hours prior to magrolimab dosing			Within 12 hours prior to magrolimab dosing			Within 12 hours prior to magrolimab dosing for 2nd weekly dose	Within 12 hours prior to magrolimab dosing before 1st, 5th, 9th, 15th and 21st biweekly maintenance doses of 30 mg/kg[d]
Antidrug antibodies[e]								
Magrolimab Administration								
Premedication	X		X	X	X			
Magrolimab[g]	X		X	X	X	X	X	X

ADA = antidrug antibodies; PK = pharmacokinetic(s)

a In cases of magrolimab repriming/re-escalation following a treatment delay (Protocol Amendment 5 Section 5.8.1), follow magrolimab schedule of assessment and administration for repriming Appendix Table 6.

b Vital signs will be assessed prior to administration of magrolimab. Details are provided in Protocol Amendment 5 Section 6.4.5.

c Hemoglobin must be performed within 24 hours prior to magrolimab dosing on Days 1 and 4 to ensure hemoglobin is ≥ 9 g/dL. Patients who do not meet these criteria must be transfused and have their hemoglobin rechecked to meet 9 g/dL prior to each of the first 2 magrolimab doses. Hemoglobin must be checked again 3 to 6 hours after the initiation of the first and second doses of magrolimab during initial treatment (see Protocol Amendment 5 Section 5.8).

d On the first day of the biweekly maintenance dose, an additional sample for postdose PK will be collected at 1 hour (± 15 minutes) after the end of infusion of magrolimab.

e When collected on the day of study treatment dosing, the blood sample for ADA must be collected at the same time as the predose PK sample. Antidrug antibodies will not be collected on Day 8.

f Premedication for magrolimab is required prior to the administration of the first 4 doses of study treatment and in case of reintroduction with repriming. Premedication for subsequent doses may be continued based on the treating physician's clinical judgment and the presence/severity of prior infusion related reactions. In the case of a Grade 3 infusion related reaction, a premedication regimen for subsequent doses is required (Protocol Amendment 5 Section 7.8.1.2).

g Magrolimab should not be given on consecutive days. The duration of infusion will be 3 hours (± 30 minutes) for the first 3 doses of magrolimab, and then 2 hours (± 30 minutes) for infusions beyond the first 3 doses. Monitor patients for 1 hour post infusion for priming, repriming/re-escalation, and maintenance doses during the first 4 weeks. For magrolimab dosing, refer to Protocol Amendment 5 Table 2.

Appendix Table 4. Schedule of Assessments - Treatment Period for the 7 + 3 Regimen

Visit Window	Induction Cycle(s)										Consolidation Cycles (up to 4 cycles)				
	None		± 3[a] Days								± 3[a] Days				
Cycle Day	1	2	3	4	5	6	7	15	21 and Twice Weekly Thereafter Until Count Recovery or Day 56, Whichever Occurs First	At Count Recovery[b]	1	3	5	21 and Weekly Thereafter Until Count Recovery or Day 56, Whichever Occurs First	At Count Recovery[b]
PRO Assessment[c]	X										X				
Serum or urine Pregnancy Test[d]	X										X				
CBC with Differential, Platelets, Reticulocytes, Blasts[e,f]	X	X		X			X	X	X	X	X			X	X
12-lead ECG (single)															X[g]
Echocardiogram or MUGA															X[g]
Haptoglobin and LDH[e]	X						X				X				
Serum or Plasma Chemistry[e]	X						X	X	X	X	X			X	X
Peripheral Blood Smear (for General Morphology)[e,h]	X	X						X							
Peripheral Blood Smear (for Blasts)[b, i]								X[i]		X					X
Buccal Swab[k]	X														
Peripheral Blood Sample for Correlative Studies[l]	X							X[j]		X					Consolidation C4 only

Visit Window	Induction Cycle(s)										Consolidation Cycles (up to 4 cycles)				
	None		± 3[a] Days								± 3[a] Days				
Cycle Day	1	2	3	4	5	6	7	15	21 and Twice Weekly Thereafter Until Count Recovery or Day 56, Whichever Occurs First	At Count Recovery[b]	1	3	5	21 and Weekly Thereafter Until Count Recovery or Day 56, Whichever Occurs First	At Count Recovery[b]
Peripheral Blood Sample for MRD Assessment[b]								X[j]		X					X
Bone Marrow Aspirate for Cytogenetics, MRD Monitoring and Response Assessment[b,i,m]								X[j]		X					X
Bone Marrow Aspirate and Biopsy for Correlative Studies[n]										X					Consolidation C4 only
Vital Signs[o]	X	X	X	X	X	X	X	X	X	X	X			X	X
Weight[o]	X										X				
Symptom-Directed Physical Examination[e]	X						X	X		X	X				X
Adverse Events, Concomitant Medications (Including Blood Transfusions)[p]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Visit Window	Induction Cycle(s)										Consolidation Cycles (up to 4 cycles)				
	None		± 3[a] Days								± 3[a] Days				
Cycle Day	1	2	3	4	5	6	7	15	21 and Twice Weekly Thereafter Until Count Recovery or Day 56, Whichever Occurs First	At Count Recovery[b]	1	3	5	21 and Weekly Thereafter Until Count Recovery or Day 56, Whichever Occurs First	At Count Recovery[b]
Study Treatment Administration															
7 + 3															
Daunorubicin or Idarubicin[q]	X	X	X												
Cytarabine[r]	X	X	X	X	X	X	X								
5 + 2															
Daunorubicin or Idarubicin[q]	X	X													
Cytarabine[r]	X	X	X	X	X										
Consolidation															
Cytarabine (HiDac)[s]											X	X	X		

C = cycle; CBC = complete blood count; ECG = electrocardiogram; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core Questionnaire; EQ-5D-5L = 5-level EuroQol 5 dimensions; LDH = lactate dehydrogenase; MRD = minimal residual disease; MUGA = multigated acquisition (scan); PGIC = Patient Global Impression of Change; PGIS = Patient Global Impression of Severity; PRO = patient-reported outcome; WBC = white blood cell

a ± 3-day visit window does not apply to specimen collection during induction for correlative studies, nor to study drug administration.

b Response assessments will be performed as described in Protocol Amendment 5 Table 13.

c Four PRO instruments will be administered in this study: the EORTC QLQ-C30 questionnaire, the EQ-5D-5L, the PGIS, and the PGIC. The patient should complete these questionnaires before any other study procedures at required visits. EORTC QLQ-C30 and EQ-5D-5L questionnaires should be performed prior to PGIS/PGIC. PGIC is not required at Cycle 1 Day 1.

d Screening pregnancy test may be used if performed within 72 hours of first dose; pregnancy tests will be conducted on Day 1 of every cycle; additional guidance is provided in Protocol Amendment 5 Section 6.4.1.

e Pretreatment assessments for the initial dose (Cycle 1 Day 1) may be collected up to 72 hours before administration of any study treatment; thereafter, pretreatment assessments are to be collected within 24 hours prior to any intravenous or subcutaneous study drugs during the first 2 weeks and within 72 hours prior to any intravenous or subcutaneous study drugs thereafter.

f Additional samples for CBC may be collected outside of the protocol-specified time points to ensure a WBC level ≤ 20 × 10^3/μL prior to initiation of study treatment.
g At the end of Consolidation Cycles 1 and 4.
h Peripheral blood smears will be collected at predose and assessed locally.
i A bone marrow sample is to be collected for response assessment. An aspirate sample will be collected for response assessment and MRD assessment. Response assessments may be adjusted by ± 5 days for Cycle 1 (Day 15). The window for post consolidation or post transplantation is ± 14 days.
j Response assessment (including bone marrow biopsy/aspirate) at C1D15 should be performed only after 7 + 3 induction to determine if second induction with 5 + 2 is needed. After 5 + 2 induction, there is no need to perform Day 15 bone marrow assessment and bone marrow assessment should be performed only at count recovery (not beyond 42 days after the initiation of 5 + 2).
k Single sample to be collected on Day 1 of the first induction cycles or at any time during the study.
l Samples will be collected predose within 12 hours prior to study treatment administration. Collection of peripheral blood for correlative studies will be allowed within 7 days (rather than a 3-day window).
m Conventional cytogenetics to be tested per institutional standards.
n Collection of bone marrow aspirate and biopsy for correlative studies will be allowed within 7 days (rather than a 3-day window).
o Vital signs will be assessed prior to infusion of each study treatment. Weight will be assessed on Day 1 of each cycle. Details are provided in Protocol Amendment 5 Section 6.4.5.
p Collected at all regularly scheduled visits.
q For 7 + 3 regimen, daunorubicin or idarubicin is administered on Days 1-3 and for 5 + 2 regimen, daunorubicin or idarubicin is administered on Days 1 and 2.
r For 7 + 3 regimen, cytarabine is administered on Days 1-7 and for 5 + 2 regimen, cytarabine is administered on Days 1-5.
s Cytarabine (HiDAC) is administered every 12 hours in the consolidation cycles.

Appendix Table 5. Schedule of Assessments – Post treatment

	End of Treatment Visit	Safety Follow-up Visit/Call (Telephone)[a]	Safety Follow-up Visit/Call (Telephone)[a]	Long -term Follow-up	Long-term Follow-up After SCT	Survival Follow-up
	Within 7 Days After Last Dose or EOT Decision, Whichever Occurs Later	30 Days After Last Dose	70 Days After Last Dose[b]	Until Disease Progression or Start of New Anti-AML Therapy[c], Whichever Occurs First[d]	Until Disease Progression[b] or Start of a New Anti-AML Therapy[c], Whichever Occurs First[d]	Every 2 Months Until Death or End of Study
Visit Window	**± 7 Days**	**± 7 Days**	**± 7 Days**	**± 14 Days**	**± 14 days**	
Serum or Urine Pregnancy Test[e]	Q4W	→	→	→	→	→
CBC with Differential, Platelet Count, Reticulocytes, Blasts	X			Q12W	Q12W	
Serum or Plasma Chemistry	X					
Peripheral Blood for Correlative Studies[f]	X					
Pharmacokinetics	X					
Antidrug Antibodies	X					
Bone Marrow Aspirate[i] for MRD Monitoring, Response Assessment[g], and Cytogenetics[h]	X[i]			Q12W	Q12W	
Peripheral Blood Smear (for Blasts)[g]	X[e]			Q12W	Q12W	
12-lead ECG (single) (for patients treated with 7 + 3)[j]	X			Q12W	Q12W	
Echocardiogram or MUGA (for patients treated with 7 + 3)[j]	X			Q12W	Q12W	
ECOG performance status	X					
Vital Signs	X					
Symptom-Directed Physical Examination	X					
PRO Assessment[k]	X				Q12W	
Adverse Events[l]	X	X	X			
Concomitant Medications	X	X	X			

	End of Treatment Visit	Safety Follow-up Visit/Call (Telephone)[a]	Safety Follow-up Visit/Call (Telephone)[a]	Long -term Follow-up	Long-term Follow-up After SCT	Survival Follow-up
	Within 7 Days After Last Dose or EOT Decision, Whichever Occurs Later	30 Days After Last Dose	70 Days After Last Dose[b]	Until Disease Progression or Start of New Anti-AML Therapy[c], Whichever Occurs First[d]	Until Disease Progression[b] or Start of a New Anti-AML Therapy[c], Whichever Occurs First[d]	Every 2 Months Until Death or End of Study
Visit Window	**± 7 Days**	**± 7 Days**	**± 7 Days**	**± 14 Days**	**± 14 days**	
New Anti-AML Therapy[m]	X	X	X	X	X	X
Survival Follow-up						X

AE = adverse event; CBC = complete blood count; CR = complete remission; CRh = complete remission with partial hematologic recovery; CRi = complete remission with incomplete count recovery; ECG = electrocardiogram; ECOG = Eastern Cooperative Oncology Group; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core Questionnaire; EOT = end of treatment; MLFS = morphologic leukemia-free state; MUGA = multigated acquisition (scan); PGIS/PGIC = Patient Global Impression of Severity/Patient Global Impression of Change; PR = partial remission; PRO = Patient Report Outcome; Q4W = every 4 weeks; Q12W = every 12 weeks; SAE = serious adverse event; SCT = stem cell transplant; SOC = standard of care

a If the patient experiences a treatment-related AE or an SAE (regardless of attribution), the patient must be asked to come to the site.
b For patients who do not initiate new anti-AML therapy after the last dose. See Protocol Amendment 5 Section 6.4.11. for adverse event reporting details.
c For patients who start new anti-AML therapy (other than SCT) before a relapse, efficacy status (done as SOC) will be collected until relapse.
d Disease progression includes relapse after CR/CRi/CRh or disease progression after PR, stable disease, or MLFS.
e Pregnancy tests should be taken at monthly intervals until end of contraception requirement.
f Peripheral blood for correlative studies should not be repeated at EOT if done at the end of the Consolidation Cycle 4.
g Response assessment at EOT is required at last dose or EOT decision (± 14 days) and is not required if performed within the last 30 days or if progressive disease has been documented or start of new anti-AML therapy, whichever comes first. (SCT and maintenance therapy are not considered new anti-AML therapy.)
h Conventional cytogenetic testing (per institutional standards) is required for all patients.
i Bone marrow aspirate and biopsy for correlative studies is required at EOT if not done at the end of the Consolidation Cycle 4.
j Only for patients undergoing treatment with 7 + 3 intensive chemotherapy. ECG and echocardiogram/MUGA should not be repeated at EOT visit if performed in the past 4 weeks.
k EORTC QLQ-C30 and EQ-5D-5L questionnaires should be performed prior to PGIS/PGIC.
l Report all AEs through the safety follow-up visit/call, and any treatment-related SAEs thereafter.
m Collect data for the first new anti-AML therapy following the last dose of study treatment.

Appendix Table 6. Schedule of Assessments - Repriming/Reescalation Cycle (Required after Magrolimab Delays of >4 Weeks)

Visit Window (Days)[a]	None			± 3				
Day	1	2	4	8	11	15	22[b]	29, then every 2 weeks OR 57, then every 2 weeks[b]
Safety								
CBC with differential, platelets, reticulocytes[c,d]	X	X	X	X	X	X	X	
Haptoglobin and LDH[c]	X	X	X	X				
Chemistry[c]	X	X	X	X		X		
Peripheral blood smear for general morphology[c,e]	X	X			X			
Vital signs[f]	X		X	X	X	X	X	X
Weight	X							
Symptom-directed physical examination[c]	X			X		X		
Adverse events[g]	→	→	→	→	→	→	→	→
Concomitant medications[g]	→	→	→	→	→	→	→	→
PK/Immunogenicity								
PK[j]	X			X			X[j]	X[j]
Antidrug antibodies[k]	X						X[k]	X[k]
Magrolimab Administration								
Premedication[l]	X		X	X	X			
Magrolimab[m]	X		X	X	X	X	X	X

ADA = antidrug antibodies; CBC = complete blood count; EOT = end of treatment; LDH = lactate dehydrogenase; PK = pharmacokinetic(s); Q4W = every 4 weeks; WBC = white blood cell

a Any other visit window specifications for individual assessments should be applied.

b In case the repriming occurs during the first 4 weeks of magrolimab treatment, patient should receive magrolimab 30 mg/kg weekly × 5 after receiving Day 15 dose. All Day 22 safety assessments should be completed weekly x 5. One week after the 5th weekly dose, dosing of magrolimab will be 30 mg/kg Q2W.

c Pretreatment assessments for the initial dose may be collected up to 72 hours before administration of any study treatment. Pretreatment laboratory assessments are to be collected within 24 hours prior to any intravenous or subcutaneous study drugs during the first 2 weeks and within 72 hours prior to any intravenous or subcutaneous study drugs thereafter.

d Additional samples for CBC may be collected outside of the protocol-specified time points to ensure a WBC level $\leq 20 \times 10^3/\mu L$ prior to each magrolimab dose during first 4 weeks of repriming. In the case of repriming, before the administration of the 2 first doses of magrolimab, hemoglobin should be ≥ 9 g/dL. Transfusions are allowed to meet this hemoglobin level.

e Peripheral blood smears for general morphology will be collected predose and assessed locally.

f Vital signs will be assessed prior to administration of magrolimab. Details are provided in Protocol Amendment 5 Section 6.4.5.

g Adverse events and concomitant medications should be recorded at all scheduled and unscheduled assessment visits, and at all treatment visits, even when other assessments are not scheduled.

j Samples will be collected within 72 hours before the first dose of magrolimab and within 12 hours before subsequent doses of magrolimab. In addition to Day 1, and Day 8, predose samples will also be collected before the Day 29 dose (only applicable if the repriming schedule has 4 additional weekly doses post Day 22), as well as before the 1st, 5th, 9th, 15th, and 21st biweekly maintenance doses of 30 mg/kg, respectively, and at EOT. On the first day of the biweekly maintenance dose, an additional sample for postdose PK will be collected at 1 hour (± 15 minutes) after the end of infusion of magrolimab.

k When collected on the day of magrolimab dosing, the blood sample for ADA must be collected at the same time as the predose PK sample. ADA samples will be collected at predose on Day 1 and Day 29 (only applicable if the repriming schedule has 4 additional weekly doses post Day 22), as well as before the 1st, 5th, 9th, 15th and 21st biweekly maintenance doses of 30 mg/kg, respectively, and at EOT.

l Premedication for magrolimab is required prior to the administration of the first 4 doses of study treatment in case of reintroduction with repriming. Premedication for subsequent cycles may be continued based on the treating physician's clinical judgment and the presence/severity of prior infusion related reactions. In the case of a Grade 3 infusion related reaction, a premedication regimen for subsequent doses is required (Protocol Amendment 5 Section 7.8.1.2).

m Magrolimab should not be given on consecutive days. The duration of infusion will be 3 hours (± 30 minutes) for the first 3 doses, and then 2 hours (± 30 minutes) for infusions beyond the first 3 doses. Monitor patients for 1 hour post infusion, during first 4 weeks for repriming. For magrolimab dosing, please refer to Protocol Amendment 5 Table 2.

Appendix Table 7. Schedule of Assessments - Treatment Period for Azacitidine (Experimental Arm) and Venetoclax + Azacitidine Regimens, in the Event the Study Meets Futility, and the Sponsor Decides to Terminate the Study

Visit Window	Cycle (28-day cycles)																																		
	Cycle 1													Cycle 2											Cycle 3+										
	None	± 3 Days												± 3 Days											± 3 Days										
Cycle Day	1	2	3	4	5	6	7	8	11	15	22	28	Twice Weekly Until Count Recovery (Max = 14 Days)[a]	1	2	3	4	5	6	7	8	15	22	28	Twice Weekly Until Count Recovery (Max = 14 Days)[a]	1	2	3	4	5	6	7	15	28	Twice Weekly Until Count Recovery (Max = 14 Days)[a]
Serum or Urine Pregnancy Test[b,]	X													X												X									
CBC with Differential, Platelets, Reticulocytes, Blasts[c, d]	X	X		X				X	X	X	X	X	X	X							X	X	X	X	X	X							X	X	X
Serum or Plasma Chemistry[e]	X[e]	X[e]	X[e]	X[e]				X		X	X			X								X				X							X		
Bone Marrow Aspirate for Response Assessment[f, g, h]												X												X										C4D28, C6D28 then Q3C	
Vital Signs[i]	X	X						X	X	X	X			X							X	X	X			X							X		
Weight[i]	X													X												X									
Symptom-directed Physical Examination[c]	X							X		X				X												X									

Visit Window	Cycle (28-day cycles)																																		
	Cycle 1													Cycle 2												Cycle 3+									
	None	± 3 Days												± 3 Days												± 3 Days									
Cycle Day	1	2	3	4	5	6	7	8	11	15	22	28	Twice Weekly Until Count Recovery (Max = 14 Days)[a]	1	2	3	4	5	6	7	8	15	22	28	Twice Weekly Until Count Recovery (Max = 14 Days)[a]	1	2	3	4	5	6	7	15	28	Twice Weekly Until Count Recovery (Max = 14 Days)[a]
Adverse Events, Concomitant Medications (Including Blood Transfusions)[j]	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	
Study Treatment Dispensing																																			
Venetoclax[k]	X													X												X									
Study Treatment Administration																																			
Azacitidine[l]	X	X	X	X	X	X	X							X	X	X	X	X	X	X						X	X	X	X	X	X	X			
Venetoclax[k, m]	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	

C = cycle; CBC = complete blood count; D = day; MRD = minimal residual disease; Q3C = every 3 cycles; SOC = standard of care; WBC = white blood cell

a. If the patient is cytopenic at Day 28, CBC is to be monitored at least twice per week for 2 weeks or until optimal count recovery is reached (whichever comes first). The best CBC result within the ± 2-week window is to be used for the response assessment, with the date of response being the date of the bone marrow assessment. Complete blood count need not be repeated if the prior CBC (including prior Day 28 CBC) is within 3 days of Day 1.

b. Screening pregnancy test may be used if performed within 72 hours of first dose; pregnancy tests will be conducted on Day 1 of every cycle; additional guidance is provided in Protocol Amendment 5 Section 6.4.1.

c. Pretreatment assessments for the initial dose (Cycle 1 Day 1) may be collected up to 72 hours before administration of any study treatment except for CBC, which must be performed within 24 hours prior to magrolimab dosing. Thereafter, pretreatment assessments are to be collected within 24 hours prior to any intravenous or subcutaneous study drugs during the first 2 weeks and within 72 hours prior to any intravenous or subcutaneous study drugs thereafter.

d. Additional samples for CBC may be collected outside of the protocol-specified time points to ensure a WBC level $\leq 20 \times 10^3/\mu L$ prior to each magrolimab dose during Cycle 1.

e. To monitor the risk of tumor lysis syndrome during venetoclax ramp-up, blood chemistry is to be collected predose and 6 to 8 hours postdose of venetoclax administration on Cycle 1 Day 1, Cycle 1 Day 2, and Cycle 1 Day 3. Blood chemistry on Cycle 1 Day 4 is to be collected 24 hours after the dose of venetoclax given on Cycle 1 Day 3.

f. Bone marrow assessments may continue locally as per the schedule outlined in Protocol Amendment 5 Table 13 and Table 26 or as per investigator discretion. MRD testing will not be required nor performed by the central laboratory but may be done locally per SOC. If continuing response assessments per Protocol Amendment 5 Table 13 and Table 26, Day 28 assessments can be done on Day 1 of the next cycle if there is no foreseen delay of more than 7 days. Bone marrow response information from Day 28 may be used to decide start of the next cycle per dosing modification guidelines in the protocol (Protocol Amendment 5 Section 5.10, and Table 8, Table 9, and Table 11).
g. Conventional cytogenetics testing may be performed locally per SOC but will not be required.
h. If continuing assessments per Protocol Amendment 5 Table 13 and Table 26, response assessments may be adjusted by up to 1 week prior to Cycle 1 Day 28, and Cycle 2 Day 28. After Cycle 2 Day 28, the window is up to 14 days ± from Day 28. Bone marrow results should be reviewed as required for determining schedule modifications.
i. Vital signs will be assessed prior to infusion/injection of each study treatment on the days marked in the table. Weight will be assessed on Day 1 of each cycle. Details are provided in Protocol Amendment 5 Section 6.4.5.
j. Collected at all regularly scheduled visits. In the event the study meets futility, and the sponsor decides to terminate the study, AEs that occur following initiation of study medication, regardless of cause or relationship, will be collected until 30 days (± 7 days) after last administration of study drug and reported on the eCRFs as instructed.
k. Venetoclax will be dispensed to the patient on Day 1 of each treatment cycle.
l. Azacitidine administration should be completed at least 1 hour before magrolimab administration on days when both drugs are administered. Azacitidine may be administered on an alternative schedule such as Days 1 to 5, Day 8, and Day 9 of a 28-day cycle for flexibility and convenience as long as the 7 doses of azacitidine of the cycle are administered within 9 consecutive days.
m. Venetoclax is administered daily. Please refer to Protocol Amendment 5 Section 5.4.

Appendix Table 8. Magrolimab Administration and Associated Assessment Schedule-Treatment Period, in the Event the Study Meets Futility, and the Sponsor Decides to Terminate the Study

Visit Window (Days)	None[a]			± 3[a]				
Day	**1**	**2**	**4**	**8**	**11**	**15**	**Weekly × 5**	**Every 2 Weeks**
Vital signs[b]	X		X	X	X	X	X	X
Hemoglobin[c]	Pre and post dose		Pre and post dose					
Magrolimab Administration								
Premedication[d]	X		X	X	X			
Magrolimab[e]	X		X	X	X	X	X	X

a. In cases of magrolimab repriming/re-escalation following a treatment delay (Protocol Amendment 5 Section 5.8.1), follow magrolimab schedule of assessment and administration for repriming (Appendix Table 6).
b. Vital signs will be assessed prior to administration of magrolimab. Details are provided in Protocol Amendment 5 Section 6.4.5.
c. Hemoglobin must be performed within 24 hours prior to magrolimab dosing on Days 1 and 4 to ensure hemoglobin is ≥ 9 g/dL. Patients who do not meet these criteria must be transfused and have their hemoglobin rechecked to meet 9 g/dL prior to each of the first 2 magrolimab doses. Hemoglobin must be checked again 3 to 6 hours after the initiation of the first and second doses of magrolimab during initial treatment (see Protocol Amendment 5 Section 5.8).
d. Premedication is required prior to the administration of the first 4 doses of magrolimab and in case of reintroduction with repriming. Premedications should include oral acetaminophen 650 to 1000 mg, oral or IV diphenhydramine 25 to 50 mg, and IV dexamethasone 4 to 20 mg or comparable regimen. For patients who do not experience an IRR with the first 2 doses of magrolimab, steroid pretreatment can be discontinued at investigators' discretion. Patients who experience IRRs with the first 2 doses of magrolimab should continue premedication with corticosteroids prior to subsequent doses at the investigator's discretion. (Protocol Amendment 5 Sections 5.9 and 7.8.1.2).
e. Magrolimab should not be given on consecutive days. The duration of infusion will be 3 hours (± 30 minutes) for the first 3 doses of magrolimab, and then 2 hours (± 30 minutes) for infusions beyond the first 3 doses. Monitor patients for 1 hour post infusion for priming, repriming/re-escalation, and maintenance doses during the first 4 weeks. For magrolimab dosing, refer to Protocol Amendment 5 Table 2.

Appendix Table 9. Schedule of Assessments – Posttreatment, in the Event the Study Meets Futility, and the Sponsor Decides to Terminate the Study

	End of Treatment Visit	Safety Follow-up Visit/Call (Telephone)
	Within 7 Days After Last Dose or EOT Decision, Whichever Occurs Later	30 Days After Last Dose
Visit Window	**± 7 Days**	**± 7 Days**
Serum or Urine Pregnancy Test[a]	Q4W	
CBC with Differential, Platelet Count, Reticulocytes, Blasts	X	
Serum or Plasma Chemistry	X	
Bone Marrow Aspirate for Response Assessment[b, c]	X	
ECOG performance status	X	
Vital Signs	X	
Symptom-Directed Physical Examination	X	
Adverse Events[d, e]	X	X
Concomitant Medications	X	X

AE = adverse event; CBC = complete blood count; ECOG = Eastern Cooperative Oncology Group; EOT = end of treatment; MRD = minimal residual disease; Q4W = every 4 weeks; SAE = serious adverse event; SCT = stem cell transplant; SOC = standard of care

a. Pregnancy tests should be taken at monthly intervals until end of contraception requirement (Protocol Amendment 5 Appendix 5).
b. Response assessment at EOT may be performed locally at last dose or EOT decision (± 14 days). MRD testing will not be required nor performed by the central laboratory but may be done locally per SOC.
c. Conventional cytogenetic testing may be performed per SOC but is not required.
d. Report all AEs through the safety follow-up visit/call. SAEs that occur after the 30 days (± 7 days) posttreatment follow-up visit may be reported if deemed relevant to the use of study drug by the investigator. Adverse events and concomitant medications should be recorded at all scheduled and unscheduled assessment visits, and at all treatment visits, even when other assessments are not scheduled. In the event the study meets futility and the sponsor decides to terminate the study, AEs and concomitant medications will be collected until 30 days (± 7 days) after last administration of study drug and reported on eCRFs as instructed. Post-study anti-AML therapy status will not be collected for patients discontinuing study treatment in the event of study termination due to futility.
e. If the patient experiences a treatment-related AE or an SAE (regardless of attribution), the patient must be asked to come to the site. In the event the study meets futility, and the sponsor decides to terminate the study, SAEs that occur after the 30 days (± 7 days) posttreatment follow-up visit may be reported if deemed relevant to the use of study drug by the investigator.

Appendix Table 10. Schedule of Assessments - Repriming/Re-escalation Cycle (Required after Magrolimab Delays of > 4 Weeks), in the Event the Study Meets Futility, and the Sponsor Decides to Terminate the Study

Visit Window (Days)[a]	None			± 3				
Day	1	2	4	8	11	15	22[b]	29, then every 2 weeks OR 57, then every 2 weeks[b]
Safety								
CBC with differential, platelets, reticulocytes[c,d]	X	X	X	X	X	X	X	
Chemistry[c]	X	X	X	X		X		
Vital signs[e]	X		X	X	X	X	X	X
Weight	X							
Symptom-directed physical examination[c]	X			X		X		
Adverse events[f]	→							→
Concomitant medications[f]	→							→
Magrolimab Administration								
Premedication[g]	X		X	X	X			
Magrolimab[h]	X		X	X	X	X	X	X

CBC = complete blood count; Q2W = every 2 weeks; WBC = white blood cell

a. Any other visit window specifications for individual assessments should be applied.
b. In case the repriming occurs during the first 4 weeks of magrolimab treatment, patient should receive magrolimab 30 mg/kg weekly × 5 after receiving Day 15 dose. All Day 22 safety assessments should be completed weekly × 5. One week after the 5th weekly dose, dosing of magrolimab will be 30 mg/kg Q2W.
c. Pretreatment assessments for the initial dose may be collected up to 72 hours before administration of any study treatment. Pretreatment laboratory assessments are to be collected within 24 hours prior to any intravenous or subcutaneous study drugs during the first 2 weeks and within 72 hours prior to any intravenous or subcutaneous study drugs thereafter.
d. Additional samples for CBC may be collected outside of the protocol-specified time points to ensure a WBC level $\leq 20 \times 10^3/\mu L$ prior to each magrolimab dose during first 4 weeks of repriming. In the case of repriming, before the administration of the 2 first doses of magrolimab, hemoglobin should be ≥ 9 g/dL. Transfusions are allowed to meet this hemoglobin level.
e. Vital signs will be assessed prior to administration of magrolimab. Details are provided in Protocol Amendment 5 Section 6.4.5.
f. Adverse events and concomitant medications should be recorded at all scheduled and unscheduled assessment visits, and at all treatment visits, even when other assessments are not scheduled. In the event the study meets futility, and the sponsor decides to terminate the study, AEs and concomitant medications will be collected until 30 days (± 7 days) after last administration of study drug and reported on eCRFs as instructed. Post-study anti-AML therapy status will not be collected for patients discontinuing study treatment in the event of study termination due to futility.

g. Premedication for magrolimab is required prior to the administration of the first 4 doses of study treatment in case of reintroduction with repriming. Premedications should include oral acetaminophen 650 to 1000 mg, oral or IV diphenhydramine 25 to 50 mg, and IV dexamethasone 4 to 20 mg or comparable regimen. For patients who do not experience an IRR with the first 2 doses of magrolimab, steroid pretreatment can be discontinued at investigators' discretion. Patients who experience IRRs with the first 2 doses of magrolimab should continue premedication with corticosteroids prior to subsequence doses at the investigator's discretion (Protocol Amendment 5 Sections 5.9 and 7.8.1.2)
h. Magrolimab should not be given on consecutive days. The duration of infusion will be 3 hours (± 30 minutes) for the first 3 doses, and then 2 hours (± 30 minutes) for infusions beyond the first 3 doses. Monitor patients for 1 hour post infusion, during first 4 weeks for repriming. For magrolimab dosing, please refer to Protocol Amendment 5 Table 2

Appendix 2. Details for Futility Interim Analysis

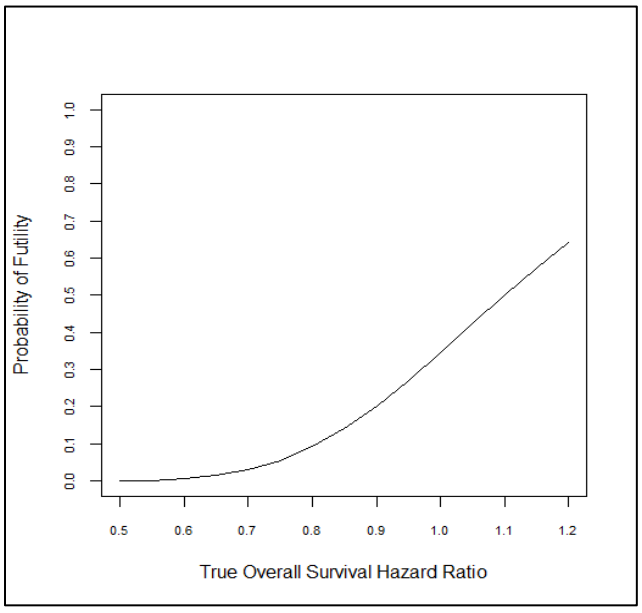
This appendix provides additional details for the planned interim futility analysis of study GS-US-546-5857.

The planned futility interim analysis will be performed after approximately 69 deaths (40% of the expected 171 OS events) in the stratum of patients appropriate for non-intensive therapy have occurred. The analysis will include a stratified log-rank test for OS in the stratum of patients appropriate for nonintensive therapy and will be reviewed by the DMC. A non-binding futility rule with a boundary HR = 1.1 will be implemented. The DMC may make a recommendation to terminate the study for futility if the observed HR for the OS in patients appropriate for non-intensive therapy is larger than 1.1.

Predictive power is defined as a weighted average of the conditional power; the weighting function is determined by the sampling distribution of the observed HR based on the data at the interim analysis {Lan 2012}. When exactly 69 OS events are observed at the interim and assuming a non-informative prior, this futility rule of an OS HR > 1.1 corresponds to observing a predictive power < 1.7 % in the ITT population of patients appropriate for non-intensive therapy.

Appendix Figure 1 presents the operating characteristics of futility rule with the boundary of 1.1 at the interim of 69 OS events. When the true OS HR in patients appropriate for non-intensive therapy is 0.74, the probability of observing HR > 1.1 at the interim analysis is less than 5%. On the other hand, when the true hazard ratio is 1, indicating lack of efficacy, the probability of observing HR > 1.1 at the interim analysis is 35%.

Appendix Figure 1. Probability of Observing Overall Survival Hazard Ratio >1.1



GS-US-546-5857-SAP-Final Analysis

ELECTRONIC SIGNATURES

Signed by	Meaning of Signature	Server Date (dd-MMM-yyyy hh:mm:ss)
PPD	Biostatistics eSigned	08-May-2024 06:07:29
PPD	Global Development Lead (GDL) eSigned	08-May-2024 18:00:51