STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 1b Trial of Magrolimab Monotherapy or Magrolimab in Combination with Azacitidine in Patients with Hematological Malignancies
Name of Test Drug:	Magrolimab (previously known as Hu5F9-G4)
Study Number:	5F9005
Protocol Version (Date):	Amendment 9 (21 July 2022)
Analysis Plan Version:	3.0
Analysis Plan Date:	06 February 2023
Analysis Plan Author(s):	PPD

CONFIDENTIAL AND PROPRIETARY INFORMATION

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LIST OF ABBREVIATIONS

ADA	anti-drug antibody
AE	adverse event
ALT	alanine aminotransferase
AML	acute myeloid leukemia
AST	aspartate aminotransferase
BLQ	below the limit of quantitation
BMI	body mass index
BSA	body surface area
CI	confidence interval
CR	complete remission
CRF	case report form
CSR	clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
DCR	duration of complete remission
DOR	duration of response
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
EFS	event-free survival
FAS	Full Analysis Set
FAB	French-American-British
HLT	high-level term
IPSS-R	revised international prognostic scoring system
KM	Kaplan-Meier
LLT	lower-level term
LOQ	limit of quantitation
MDS	myelodysplastic syndrome
MedDRA	Medical Dictionary for Regulatory Activities
MRD	minimal residual disease
ORR	Objective response rate
PFS	progression-free survival
PK	pharmacokinetic
PT	preferred term
Q1, Q3	first quartile, third quartile
OS	overall survival
R/R	relapse/refractory
RO	receptor occupancy
SAE	serious adverse event
SAP	statistical analysis plan
SE	Standard error

SCT	stem cell transplant
StD	standard deviation
SOC	system organ class
TEAE	treatment-emergent adverse event
TFLs	tables, figures, and listings
TN/U	treatment naïve/unfit
TTR	time to response
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) in the clinical study report (CSR) for Study 5F9005. This SAP is updated based on 5F9005 SAP Version 2.0 and the study protocol amendment 9 dated 21 July 2022. Any changes made after the finalization of the SAP will be documented in the CSR.

The pharmacodynamics analysis will be described in a separate document.

Analysis methods specified in this document take precedence over those described in protocol should there be any difference.

1.1. Study Objectives

The primary objectives of this study are as follows:

- To confirm the safety and tolerability of magrolimab monotherapy in relapsed/refractory (R/R) acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) and of magrolimab in combination with azacitidine in previously untreated patients with AML or MDS and patients with R/R AML and MDS

- To evaluate the safety, tolerability, and efficacy of magrolimab monotherapy in R/R AML/MDS, and of magrolimab in combination with azacitidine in previously untreated patients with AML/MDS or R/R AML/MDS as measured by complete remission (CR) rate for patients with AML and higher-risk MDS

- To evaluate the safety, tolerability, and efficacy of magrolimab monotherapy or in combination with azacitidine in low-risk MDS patients as measured by RBC transfusion independence rate

The secondary objectives of this study are as follows:

- To evaluate the pharmacokinetic (PK) profile of magrolimab alone and in combination with azacitidine

- To evaluate the immunogenicity of magrolimab

- To evaluate the efficacy of magrolimab alone or in combination with azacitidine as measured by duration of CR (DCR); objective response rate (ORR); CR with partial hematologic recovery; duration of response (DOR) for patients with AML; DCR for higher-risk MDS; ORR and DOR for patients with MDS; RBC transfusion independence; mean hemoglobin increase on treatment; progression-free survival (PFS); relapse-free survival (RFS), event-free survival (EFS); and overall survival (OS)

- To assess the level of minimal residual disease (MRD) negativity

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1.2. Study Design

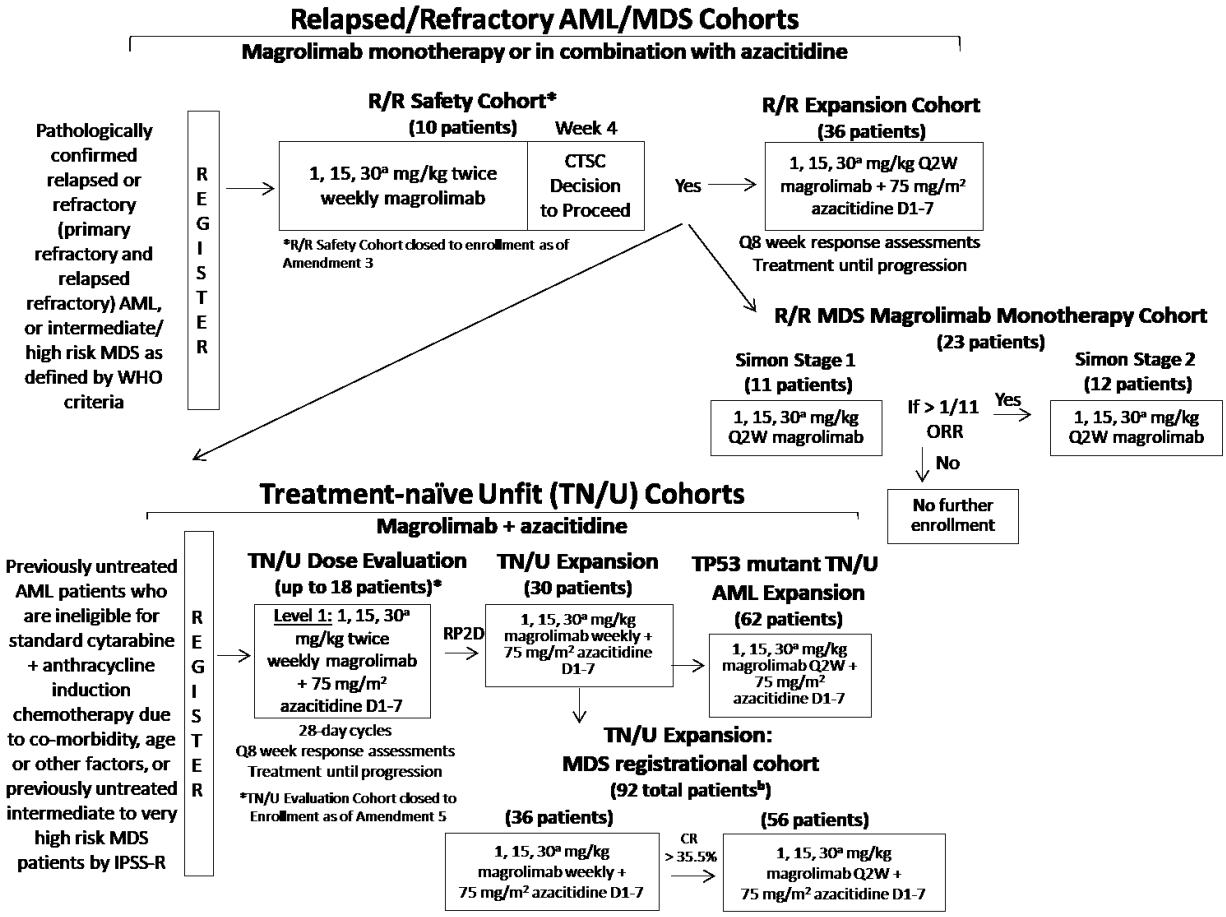
This trial is an open label, multicenter Phase 1b trial investigating the following:

- Magrolimab monotherapy or in combination with azacitidine in patients with R/R AML or MDS (including R/R low-risk RBC transfusion dependent MDS patients)
- Magrolimab in combination with azacitidine in newly diagnosed intermediate/high/very high-risk MDS patients
- Magrolimab in combination with azacitidine in newly diagnosed AML patients ineligible for standard induction chemotherapy (including TP53 mutant AML)
- Magrolimab monotherapy or in combination with azacitidine for RBC transfusion-dependent low-risk MDS patients

The study includes 4 groups of patients:

- **R/R Cohorts:** R/R AML or MDS patients who have not previously received magrolimab, who will receive magrolimab monotherapy in the safety run-in cohort or magrolimab monotherapy in the R/R MDS Magrolimab Monotherapy Cohort, and who will receive magrolimab in combination with azacitidine in the R/R expansion cohort on this study. The R/R MDS Magrolimab Monotherapy Expansion Cohort has been added to further define the activity of magrolimab alone in MDS.
- **Treatment-naïve/Unfit (TN/U) Cohorts:** AML patients ineligible for standard induction chemotherapy or previously untreated intermediate/high/very high-risk MDS patients by Revised International Prognostic Scoring System (IPSS-R) {Greenberg 2012}, who will receive magrolimab in combination with azacitidine on this study. A subcohort of untreated AML patients ineligible for standard induction chemotherapy that have a TP53 gene mutation is included here.
- **RBC Transfusion-dependent Low risk MDS Cohort:** RBC transfusion-dependent very low- to low risk MDS patients by IPSS-R who are either of the following:
  - relapsed/refractory/intolerant to or ineligible for erythropoiesis-stimulating agents (ESA) therapy
  - have a deletion in chromosome 5q who are relapsed/refractory/intolerant to or ineligible for lenalidomide therapy
- **Rollover Cohort:** Patients who received magrolimab in the Phase 1 R/R AML study (SCI-CD47-002), who will continue magrolimab monotherapy on this study.

Figure 1. Study Schema: Relapsed/Refractory and TN/U Cohorts



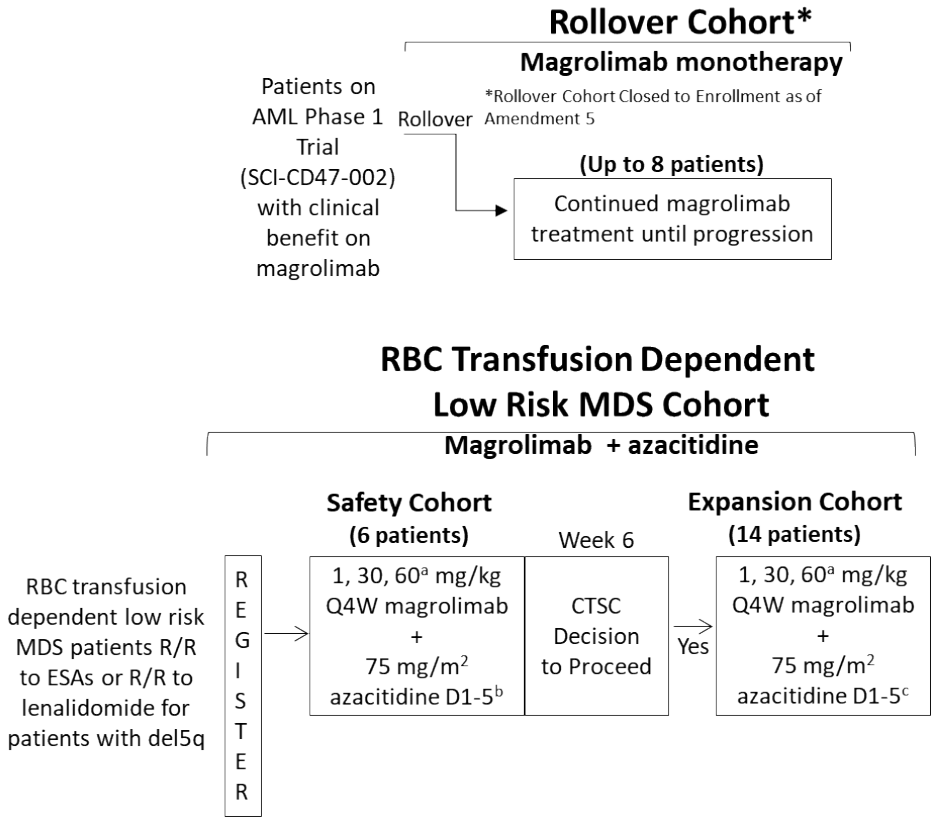
Abbreviations: AML = acute myeloid leukemia; CTSC = Clinical Trial Steering Committee; D = day; IPSS-R = Revised International Prognostic Scoring System; MDS = myelodysplastic syndrome; Q2W = every 2 weeks; Q8 week = every 8 weeks; R/R = relapsed/refractory; TN/U = treatment-naïve/unfit; WHO = World Health Organization

a Dosing will be 1 mg/kg twice weekly for 1 week (Cycle 1 Days 1 and 4) followed by 15 mg/kg on Cycle 1 Day 8; then 30 mg/kg twice weekly from Cycle 1 Day11 and thereafter for R/R Safety Cohort or 30 mg/kg on Cycle 1 Days 11, 15, and 22; then 30 mg/kg QW in Cycle 2 (Days 1, 8, 15, and 22); then Q2W (Days 1, 15) starting Cycle 3 and thereafter, as per dosing schedule for other cohorts..

b There will be approximately 92 MDS patients in total, inclusive of those 16 MDS patients treated in the original 30-patient TN/U Expansion Cohort.

As of Amendment 3 dated as 06 March 2018, the recommended Phase 2 dose and regimen (RP2DS) and the recommended dose for the cohort was determined to be magrolimab dosing at 1 mg/kg on Days 1 and 4; 15 mg/kg on Day 8; 30 mg/kg on Days 11, 15, and 22; and 30 mg/kg QW Cycle 2 and beyond. As of Amendment 6, the RP2DS, as selected by the CTSC in November 2019, was determined to be magrolimab dosing at 1 mg/kg on Days 1 and 4; 15 mg/kg on Day 8; 30 mg/kg on Days 11, 15, and 22; 30 mg/kg QW for Cycle 2; and 30 mg/kg Q2W starting Cycle 3 and thereafter.

Figure 2. Study Schema: Rollover AML and RBC Transfusion-dependent Low-risk MDS Cohorts



Abbreviations: AML = acute myeloid leukemia; CTSC = Clinical Trial Steering Committee; D =day; del5q = deletion in chromosome 5q; ESA = erythropoiesis-stimulating agent; MDS = myelodysplastic syndrome; Q4W = every 4 weeks; R/R = relapsed/refractory; TN/U = treatment-naïve/unfit; RBC = red blood cell

a Dosing will be 1 mg/kg on Cycle 1 Day 1; 30 mg/kg on Cycle 1 Days 8, 15, and 22; and 60 mg/kg Q4W starting Cycle 2 and thereafter.

b The safety cohort will be treated with magrolimab monotherapy. For patients who do not respond after Cycle 2, azacitidine may be added on subsequent cycles.

c The expansion cohort will be treated with magrolimab or magrolimab+azacitidine based on CTSC evaluation of the safety cohort.

1.3. Sample Size and Power

The number of patients planned for inclusion in this trial is up to a total of approximately 287 patients evaluable for efficacy, as follows:

- R/R Safety Cohort: 10 patients
- R/R Expansion Cohort: Up to 36 patients
- R/R MDS Magrolimab Monotherapy Cohort: 23 patients
- TN/U Dose Evaluation Cohort: Up to 18 patients

- TN/U Expansion Cohort: Up to 172 patients, including
  - Original 30 TN/U Expansion (enrolled 18 AML and 16 MDS patients, including 4 replacement patients)
  - At least 92 MDS patients (including the original 16 MDS patients enrolled in the original TN/U Expansion), of whom at least 56 patients will be on Q2W dosing. The overall MDS expansion to 92 patients will be considered for TN/U MDS.
  - Up to 62 TP53 mutant AML patients (i.e., 12 original TP53 mutation AML patients, plus 20 additional TP53 mutant AML patients added per CTSC decision in September 2019, plus 30 additional TP53 mutant AML patients per CTSC decision July 2020)
- RBC Transfusion-dependent Low-risk MDS Cohort: Up to 20 patients
- Rollover Cohort: Up to 8 patients

For the R/R Safety Cohort and Expansion Cohort, approximately 46 patients may be enrolled, including 10 patients treated in the safety run-in cohort and 36 patients treated in the expansion cohort. For the R/R Safety Cohort, 10 patients were enrolled, and this cohort was closed to further enrollment as of Amendment 3. Based on safety and efficacy data, the CTSC may decide to expand the R/R Expansion Cohort to include additional patients. An ORR of 17% has been reported in patients with R/R AML who have been treated with azacitidine {Itzykson 2015}. For an estimated response rate of 33% or higher, 36 patients would provide a 95% confidence interval, with the lower bound to exclude 18.6%, the azacitidine monotherapy efficacy rate.

Per FDA feedback, a magrolimab monotherapy cohort in R/R MDS will be evaluated to further define the activity of magrolimab to the contribution of magrolimab+azacitidine in MDS to support a potential single-arm approval of magrolimab+azacitidine in MDS. Patients will be enrolled in a Simon's 2-stage design. With a 1-sided significance level of 0.05 and 80% power, the null hypothesis that the magrolimab monotherapy ORR is 9% will be tested against the alternative of 30%. In the first stage, 11 patients will be enrolled. If there are 1 or fewer responses observed in these 11 patients, the cohort will be stopped. Otherwise, 12 additional patients will be accrued, for a total of 23. This cohort was stopped after 11 patients enrolled per CTSC decision in October 2020. The null hypothesis will be rejected if 5 or more responses are observed in 23 patients.

For the TN/U Dose Evaluation Cohort, up to 18 patients can be enrolled based on a 3+3 dose de-escalation design assuming 3 potential dose cohorts with a maximum of 6 patients treated per cohort. For the TN/U Dose Evaluation Cohort, 8 patients were enrolled, and this cohort was closed to further enrollment as of Amendment 5.

For the TN/U Expansion Cohort, a total of up to 172 patients may be enrolled. An initial sample size of 30 patients was proposed so that the 95% confidence interval of the desired 35% or higher CR rate would exclude a known CR rate of 17.85% for azacitidine alone. This sample size calculation was based on inclusion of both TN/U AML and higher-risk MDS patients. For the higher-risk, untreated, MDS-only Expansion Cohort added in Amendment 5 (16 originally

enrolled MDS patients + 76 additional patients for n = 92), an evaluation will occur after 36 patients have reached the first response assessment (Cycle 3 Day 1); however, enrollment will continue and will not be paused in the interim. A sample size of 36 patients provides 80% power to reject the null hypothesis that the CR rate is 16.5% or lower at 2-sided 0.05 significant level, assuming the true magrolimab+azacitidine CR rate is at least 35.5% (19% improvement). The null CR rate of 16.5% is based on the pivotal randomized trial leading to azacitidine approval in MDS reanalyzed by IWG 2000 criteria ({Silverman 2006}, where the upper bound of the 1-sided 95% confidence interval for azacitidine CR rate is 16.5%, with a point estimate of 10%. Based on Amendment 6, per discussion with the FDA in November 2019, the primary endpoint for this untreated, higher-risk MDS cohort was changed from CR+PR to CR rate to support a potential single-arm approval. In accordance with this CR endpoint and a transition to a Q2W magrolimab dosing regimen, a cohort of 56 patients at Q2W magrolimab dosing was added. A sample size of 56 patients provides 80% power to reject the null hypothesis that the CR rate is 16.5% or lower at a 2-sided 0.05 significant level, assuming the true CR rate is at least 31.5% (i.e., a 15% improvement). A combined planned sample size of 92 patients for the MDS Registrational Cohort will provide an 80% power to reject the updated null CR rate of 23.5% at a 2-sided 0.05 significant level, assuming the true magrolimab+azacitidine CR rate is 36.5%.

Per the CTSC decision in September 2019 and Amendment 6, a subcohort of TP53 mutant TN/U AML patients was added. Initially, 12 patients and then an additional 20 patients will be enrolled. Analysis of these patients will include all TP53 mutant patients meeting subcohort eligibility criteria enrolled prior to the Amendment/CTSC decision. A sample size of 32 patients was selected to evaluate the initial efficacy of magrolimab+azacitidine as compared to available therapies (most notably venetoclax+hypomethylating agents) in TP53 mutant AML. While venetoclax in combination with hypomethylating agents (azacitidine or decitabine) is approved in newly diagnosed AML patients who are ineligible for intensive chemotherapy, its efficacy in TP53 mutant AML patients is limited. Per a recent report, the CR+ complete remission with incomplete blood count recovery (CRi) rate of venetoclax+hypomethylating agent in TP53 mutant AML was 47% with a median duration of CR of 5.6 months and a median overall survival of 7.2 months {DiNardo 2019}. In contrast, in all-comer AML patients, the CR+CRi rate was 67% with a median duration of CR of 11.3 months and a median overall survival of 17.5 months. Assuming an observed magrolimab+azacitidine ORR of 59% for a sample size of 32 patients, the 1-sided 90% confidence interval will have a lower bound of 46.5%, which excludes a control ORR of 46%. Based on emerging data, the CTSC may decide to enroll additional patients for further safety, efficacy, or dosing information. Per CTSC decision in July 2020 and captured in Amendment 7, an additional 30 TP53 mutant AML patients were enrolled for the TN/U Expansion TP53 AML Cohort (n = 62).

For the RBC Transfusion-dependent Low-risk MDS Cohort, approximately 20 patients will be enrolled. Initially, 6 patients will be enrolled with a safety evaluation after all 6 patients complete at least Cycle 2 Day 15 treatment. This safety evaluation is being conducted given that a 60 mg/kg dose of magrolimab will be administered starting in Cycle 2, of which this highest dose has not yet been tested in patients. However, an equivalent dose of 60 mg/kg given in 1 week (30 mg/kg twice weekly) has already been administered to MDS and AML patients in this trial and has been well tolerated. The CTSC will then evaluate based on the aggregate safety profile in these 6 patients and determine whether enrollment should proceed to the remaining

14 patients. If so, these 14 patients can be simultaneously enrolled. The sample size of 20 patients is to be enrolled to evaluate an initial efficacy signal in this population, with further enrollment based on this signal. Based on emerging data, the CTSC may decide to enroll additional patients for further safety, efficacy, or dosing information. These may be enrolled as either magrolimab monotherapy or in combination with azacitidine. Patients may have their magrolimab dose interval changed (i.e., to more frequent [Q2W] or less frequent [> Q4W]) at any time on therapy based on CTSC recommendations or Sponsor requirement.

For the Rollover Cohort, 1 eligible patient from the Phase 1 study (SCI-CD47-002) is now enrolled in this study, and this cohort was closed to further enrollment as of Amendment 3.

2. TYPE OF PLANNED ANALYSIS

2.1. Primary Analysis

When all the subjects of the TN/U MDS have at least 12 months of efficacy follow-up from their first response assessments at the beginning of Cycle 3, or have discontinued from the study, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized, the primary analysis of the data will be performed.

2.2. Follow-up Analysis

After the primary analysis, additional supplemental analyses of efficacy and safety may be performed to satisfy regulatory requirements or to perform long-term efficacy (eg, overall survival) and follow-up safety assessments. P-values for the updated analyses of efficacy are for display purposes only, no formal hypothesis testing will be conducted.

2.3. Final Analysis

After all subjects have completed the study, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized, the final analysis of the data will be performed.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

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

All statistical tests will be 2-sided and performed at the 5% significance level unless otherwise specified.

By-subject listings will be presented for all subjects in the All Enrolled Analysis Set and sorted by 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. The treatment group to which subjects were initially assigned will be used in the listings. Age, sex at birth, race, and ethnicity will be included in the listings, as space permits.

3.1. Analysis Sets

Analysis sets define the subjects 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 subjects eligible for inclusion will be summarized.

A listing of reasons for exclusion from analysis sets will be provided by subject.

3.1.1. All Enrolled Analysis Set

All Enrolled Analysis Set includes all subjects who are enrolled into the cohorts specified in Section 1.2 based on the enrollment CRF.

3.1.2. Full Analysis Set

The Full Analysis Set (FAS) includes subjects in All Enrolled Analysis Set, who took at least 1 dose of magrolimab. For TN/U MDS, subjects who were assessed as higher MDS risk (defined as intermediate/high/very high-risk) by IPSS-R at baseline are eligible to be included in FAS. This is the primary analysis set for efficacy analyses.

3.1.3. Efficacy Evaluable Analysis Set

The Efficacy Evaluable Analysis Set includes subjects in the FAS set, who have at least 1 disease response assessment or who died before the first disease response assessment.

The Efficacy Evaluable Analysis Set is the secondary analysis set for efficacy analyses.

3.1.4. Safety Analysis Set

The Safety Analysis Set includes subjects in All Enrolled Analysis Set, who took at least 1 dose of magrolimab. This is the primary analysis set for safety analyses.

3.1.5. Pharmacokinetic Analysis Set

The Pharmacokinetic (PK) Analysis Set will include subjects in All Enrolled Analysis Set, who took at least 1 dose of magrolimab and have at least 1 detectable postdose magrolimab concentration value reported by the PK laboratory. This is the primary analysis set for all PK analyses.

3.1.6. Immunogenicity Analysis Set

The Immunogenicity Analysis Set includes subjects in All Enrolled Analysis Set, who took at least 1 dose of magrolimab and have at least 1 anti-drug antibody (ADA) sample result reported.

3.2. Subject Grouping

For TN/U MDS cohort, the analyses will be presented by total and then split by dose schedule (i.e. QW and Q2W) unless otherwise specified. Subjects with Q2W dosing schedule are defined as patients who start to receive 1 magrolimab dose every 2 weeks starting at Cycle 3. Subjects with QW dosing schedule are defined as patients who do not start 1 magrolimab dose every 2 weeks at the beginning of Cycle 3. For patients who discontinued from treatment before Cycle 3, the patients will be counted under the planned dose schedule.

PK and immunogenicity analyses might follow different grouping structure.

3.3. Strata and Covariates

This study does not use a stratified randomization schedule when enrolling subjects.
No covariates will be included in efficacy and safety analyses.

3.4. Examination of Subject Subgroups

Subgroup analyses based on baseline characteristics will be explored for TN/U MDS cohort. The presumed prognostic baseline characteristics include the following:

- Age (< 65 years and ≥ 65 years)
- Sex (male and female)
- Race (white and all other races)
- IPSS-R for MDS Risk Category (intermediate, high, and very high)
- Baseline bone marrow blast (<=5% and >5%)

- TP53 status (mutant and wild type)
- Cytogenetics status (complex and not complex)
- Cytogenetics risk category (favorable, intermediate, and poor)
- MDS status (therapy related and non-therapy related)
- ECOG status (0, 1, and 2)

If the number of subjects in one or more subgroups is too small to conduct the analysis, some subgroups will be pooled for the analysis.

3.5. Missing Data and Outliers

3.5.1. Missing Data

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

For missing last dosing date of study drug, imputation rules are described in Section 4.2.1. The handling of missing or incomplete dates for disease diagnosis is described in Section 5.3, for date of death and the start date of new anti-cancer therapy in Section 6.2.2, for AE onset in Section 7.1.5.2, and for prior and concomitant medications in Section 7.4.

3.5.2. 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.

3.6. 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 will be derived based on date of birth and the date of the first dose of study drug administration. If complete date of birth is not available, the reported age will be used instead. If an enrolled subject was not dosed with any study drug, the enrollment date will be used instead of the Day 1 visit date. For screening failures, the date the 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 LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "< x" (where x is considered the 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 LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "> x" (where x is considered the LOQ). Values with decimal points will follow the same logic as above.

- The 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 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.

3.7. Analysis Visit Windows

3.7.1. Definition of Study Day

Study day will be calculated from the first dosing date of study drug 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 study drug administration.

3.7.2. 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 lab are provided in Table 1:

Table 1. Analysis Visit Windows for Lab

Analysis Visit	Nominal Study Day	Visit Window Study Day	
		Lower Limit	Upper Limit
Baseline			1[a]
Week 1	8	1[b]	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	xx*7+1	(xx-1)*7+1	(xx+1)*7

a Prior to first dose date time.
b Post first dose date time.

The nominal visit as recorded on the CRF will be used when data are summarized by visit. However, the following exceptions will be made:

- An unscheduled visit prior to the first dosing of study drug will be included in the calculation of the baseline value, if applicable.
- Unscheduled visits after the first dosing of study drug will be included in determining the maximum postbaseline toxicity grade.

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

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 average of the measurements for continuous data, or the measurement with the lowest severity (eg, normal will be selected over abnormal for safety findings) 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 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 for each country, investigator and overall. The summary will present the number and percentage of subjects enrolled. For each column, the denominator for the percentage calculation will be the total number of subjects analyzed for that column.

A summary of subject disposition will be provided. This summary will present the number of subjects screened, the number of subjects enrolled, and the number of subjects in each of the categories listed below:

- Safety Analysis Set
- Full Analysis Set
- Efficacy Evaluable Analysis Set
- Continuing Magrolimab
- Continuing Azacitidine
- Magrolimab discontinuation and reasons
- Azacitidine discontinuation and reasons
- Survival follow-up status
- Study discontinuation and reasons

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

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

4.2. Extent of Study Drug Exposure and Adherence

Extent of exposure to study drug will be examined by assessing the total duration of exposure to study drug and the level of adherence relative to the study drug regimen specified in the protocol. The analyses will be done for magrolimab and azacitidine separately.

4.2.1. Duration of Exposure to Study Drug

Total duration of exposure to study drug will be defined as last dosing date minus first dosing date plus 1, regardless of any temporary interruptions in study drug administration, and will be expressed in months. If the last study drug dosing date is missing,

- If the study drug is permanently withdrawn, the latest date among the study drug end date, start date of AE leading to study treatment discontinuation, clinical visit date, laboratory sample collection date, and vital signs assessment date that occurred during the on-treatment period will be used for subjects included in the final analyses or the last available date in the database snapshot for subjects who were still on treatment at the time of an interim analysis.

- If the study drug completion status is unknown, the earlier of the date of death or data cutoff date for analysis will be used.

The total duration of exposure to study drug will be summarized using descriptive statistics. Summaries will be provided for the Safety Analysis Set.

The number of cycles subjects were exposed to each study drug will be summarized using descriptive statistics, as well as the number and percentage of subjects exposed to a given cycle category (eg, ≥1, ≥2, ≥3, etc).

The number and percentage of subjects with infusion interruptions and discontinuation will be summarized.

4.2.2. Adherence to Study Drug

4.2.2.1. Average Actual Dosage

The level of adherence of each drug will be calculated based on the following formulas and summarized respectively using descriptive statistics:

- $\text{Adherence per Specified Dose Level (\%)} = \left(\frac{\text{Total Amount of Study Drug Administered}}{\text{Study Drug Prescribed to be Administered}}\right) \text{x } 100$

- $\text{Adherence of Specified Cycle (\%)} = \frac{\text{Doses (mg) Administered within Actual Cycle}}{\text{Doses (mg) Specified by Protocol within Specified Cycle}} \text{ x } 100,$

  averaged across all cycles treated

- $\text{Adherence of Average Daily Dose (\%)} = \frac{\text{Doses (mg) Administered within Actual Cycle/Actual Cycle Length}}{\text{Doses (mg) Specified by Protocol within Specified Cycle/28 Days}} \text{ x } 100,$

  averaged across all cycles treated

No formal statistical testing is planned.

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

4.3. Protocol Deviations

Subjects who did not meet the eligibility criteria for study entry, but enrolled in the study will be summarized. The summary will present the number and percentage of subjects who did not meet at least 1 eligibility criterion and the number of subjects who did not meet specific criteria based on the All Enrolled Analysis Set. A by-subject listing will be provided for those subjects 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 subjects did not meet and related comments, if collected.

Protocol deviations occurring after subjects entered the study are documented during routine monitoring. The number and percentage of subjects with important protocol deviations by deviation reason (eg, nonadherence to study drug, violation of select inclusion/exclusion criteria) will be summarized for the All Enrolled Analysis Set. A by-subject listing will be provided for those subjects with important protocol deviation.

5. BASELINE CHARACTERISTICS

5.1. Demographics and Baseline Characteristics

Subject demographic variables (ie, age, sex, race, and ethnicity) and baseline characteristics (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 using descriptive statistics for continuous variables and using number and percentage of subjects for categorical variables. The summary of demographic data will be provided for the Safety Analysis Set.

A by-subject demographic listing, including the informed consent date, will be provided by subject ID number in ascending order.

5.2. Other Baseline Characteristics

ECOG performance status will be summarized for the Safety Analysis Set and will be listed.

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).

The following disease-specific medical history will be summarized for the Safety Analysis Set. No formal statistical testing is planned.

- Time since initial AML/MDS diagnosis (months)
- Time since the most recent AML/MDS assessment (months)
- Revised International Prognostic Scoring System (IPSS-R) for MDS risk category
- AML Cytogenetic and Molecular Risk Group by European Leukemia Net (ELN) Criteria
- World Health Organization (WHO) Classification of AML/MDS
- French-American-British (FAB) Classification of AML
- Therapy-related MDS (Yes/No)
- AML/MDS status at enrollment
- RBC-transfusion Independence at Enrollment (Yes/No)
- Cytogenetic risk assessment
- TP53 mutation status

Time since initial AML/MDS diagnosis (months) will be calculated by (date of first dosing date of study drug (or enrollment date if patient is not treated with any study drug) – date of initial AML/MDS diagnosis) / 30.4375. Time since date of most recent AML/MDS assessment (months) will be calculated by (date of first dosing date of study drug (or enrollment date if patient is not treated with any study drug) – date of most recent AML/MDS diagnosis) /30.4375.

In deriving the time since AML/MDS diagnosis, the partial dates will be imputed as follows:

- If day and month are missing but year is available, then the imputed day and month will be 01 Jan.
- If day is missing but the month and year are available, then the imputed day will be the first day of the month.
- Partial date will not be imputed if the year is missing.

A by-subject listing of general medical history will be provided by subject ID number in ascending order.

5.4. Prior Anti-cancer Therapy

Number of prior regimens, time since the completion of last regimen, and time since progression in the last regiment will be using descriptive statistics based on the Safety Analysis Set. A partial completion date will be imputed using the algorithm defined in Section 5.3.

The regimens and prior therapies that the subjects received will be summarized and listed. The last regimen subjects received prior to study entry and the best response and PD to the last regimen will be summarized.

Number of subjects who received prior radiation therapy, prior cancer-related surgery, and prior transfusions within 8 weeks prior to enrollment will be summarized and listed.

6. EFFICACY ANALYSES

Response will be assessed in MDS subjects using the criteria in Appendix 1, which are based on the 2006 IWG criteria {Cheson 2006}. For AML subjects, response assessment criteria are in Appendix 2 (which are based on ELN AML recommendation {Dohner 2017}) and IWG criteria {Cheson 2003} in Appendix 3.

6.1. Primary Efficacy Endpoint

6.1.1. Definition of the Primary Efficacy Endpoint

The primary efficacy endpoint of this study for MDS registrational cohort is:

CR Rate for MDS: The CR rate is the proportion of subjects who achieve complete remission per IWG 2006 criteria {Cheson 2006} per investigator's evaluation prior to initiation of any other new anti-cancer therapy including stem cell transplant (SCT).

CR Rate for AML: The CR rate is the proportion of subjects who achieved complete remission without minimal residual disease and complete remission per ELN 2017 Recommendation {Dohner 2017} and IWG criteria {Cheson 2003} per investigator's evaluation prior to initiation of any other new anti-cancer therapy including SCT.

6.1.2. Statistical Hypothesis for the Primary Efficacy Endpoint

The primary efficacy hypothesis to be tested for TN/U MDS is:

$$H_0: \text{CR rate} = 23.5\%$$

$$H_1: \text{CR rate} \neq 23.5\%$$

6.1.3. Analyses of the Primary Efficacy Endpoint

The analyses of primary efficacy endpoint will be based on the FAS.

CR rate and 95% confidence interval will be estimated using Clopper-Pearson method. The hypothesis will be tested at 2-sided 0.05 significance level based on exact method and p value will be presented.

6.1.4. Sensitivity Analyses of the Primary Efficacy Endpoint

To assess the robustness of the primary efficacy results, CR rate will be analyzed based on the Efficacy Evaluable Analysis Set.

EFS will be analyzed without considering any other new anti-cancer therapy as a censoring factor.

CCI [redacted]

6.2. Secondary Efficacy Endpoints

6.2.1. Definition of Secondary Efficacy Endpoints

The secondary efficacy endpoints include:

DCR: The DCR is defined as the time from the date of the first CR (prior to initiation of any other new anti-cancer therapy including SCT) until the date of documented relapse disease or death from any cause, whichever occurs first. Subjects who are not observed to have relapse disease or death will be censored at their last response assessment date.

Objective Response Rate (ORR): For AML, the ORR is the proportion of subjects who achieve Complete Response (CR), CR with incomplete hematologic (count) recovery (CRi), CR with partial hematologic (count) recovery (CRh), Partial Response (PR), Morphologic Leukemia-Free State (MLFS) prior to initiation of a new anti-cancer therapy including SCT per European Leukemia Net (ELN) AML 2017 recommendations {Dohner 2017} per investigator's evaluation.

For MDS, the ORR is the proportion of subjects who achieve Complete Remission (CR), Partial Remission (PR), marrow CR or hematological improvement (HI) prior to initiation of a new anti-cancer therapy including SCT per IWG 2006 criteria {Cheson 2006} per investigator's evaluation.

Duration of Response (DOR): The DOR is measured from the time assessment criteria are first met for objective response (prior to initiation of any other new anti-cancer therapy including SCT) until the first date of documented relapse, disease progression or death. Those who are not observed to have one of these events will be censored at their last response assessment date without evidence of progression/relapse.

Overall Survival (OS): OS is measured from the date of study treatment initiation until the date of death from any cause. Those who are not observed to die during the study will be censored at their last known alive date.

Progression-free Survival (PFS): PFS is defined as the time from the date of study treatment initiation until the date of documented relapse, disease progression or death from any cause, whichever occurs first. Those who are not observed to have one of these events will be censored at their last response assessments date with evidence of no disease progression/relapse.

Event-free Survival (EFS): For AML, EFS is defined as the time from the date of study treatment initiation until the date of documented disease progression, death from any cause, or treatment failure (defined as failure to achieve CR/CRi/CRh by Cycle 5 Day 1), whichever occurs first.

For MDS, EFS is defined as the time from the date of study treatment initiation to transformation to AML or death from any cause, whichever occurs first. Patients who are not observed to have one of these events during the study will be censored at their last response assessment date with evidence of no transformation to AML.

RBC Transfusion Independence Rate: The RBC transfusion independence rate is the proportion of patients who have a 56-day or longer period with no RBC transfusions at any time between the date of study treatment initiation and treatment discontinuation among all patients who are RBC transfusion-dependent at baseline.

MRD Negative Response Rate: The MRD-negative response rate is defined as the proportion of patients who reach MRD-negative disease status prior to initiation of other new anti-cancer therapy including SCT and achieve a morphologic CR or marrow CR for MDS patients and achieve CR/CRi/CRh/MLFS for AML patients. MRD-negative disease status will be assessed using a multiparameter flow cytometry based assay performed by a central laboratory.

6.2.2. Analysis Methods for Secondary Efficacy Endpoints

ORR and the best response will be summarized by the number of subjects and the frequency. 95% CI based on Clopper-Pearson method will be presented for ORR. Any response assessments after other anti-cancer therapy including SCT will excluded from the analyses.

DCR, DOR, PFS, EFS, and OS will be analyzed using the Kaplan-Meier method. Analysis of DCR will be analyzed on patients who achieved CR prior to initiation of any other new anti-cancer therapy including SCT, and DOR will be analyzed on patients who achieved objective responses prior to initiation of any other new anti-cancer therapy including SCT. PFS, EFS, and OS will be conducted on FAS. The KM estimate of median, 95% CI of median, Q1, and Q3 will be presented. Kaplan-Meier plot will be provided when appropriate. The following censoring rules will be implemented:

For OS: if subjects are not known to be dead at the time of analysis, the subjects will be censored at the last known alive date.

For DCR, DOR, PFS, EFS, and Time to Transformation to AML (section □):

- For DCR and DOR, if subjects have only one CR or ORR prior to any other new anti-cancer therapy (if there is) without any subsequent response assessments or events, the subjects will be censored on the CR/ORR date (i.e. duration of 1 day).

- For PFS, EFS and Time to Transformation to AML, if subjects do not have any response assessment or corresponding events prior to any other new anti-cancer therapy (if there is), the subjects will be censored on Study Day 1 (i.e. duration of 1 day).

- If subjects do not have any events, the subjects will be censored at the last response assessment on or before any other new anti-cancer therapy (if there is) excluding SCT.

- If subjects are observed to have events occurred after any other new anti-cancer therapy (if there is) excluding SCT, the subjects will be censored at their last response assessment date on or before any other new anti-cancer therapy excluding SCT.

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.

When the date of initiation of any other new anti-cancer therapy 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-cancer therapy 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-cancer therapy and the year of last dose are the same.

CCI [redacted]

[redacted]

[redacted]

Time to Response (TTR): Time to response is defined as the time for the date of study treatment initiation to the date of first OR prior to any other new anti-cancer therapy including SCT.

CCI [redacted]

6.4. Changes from Protocol-Specified Efficacy Analyses

As secondary efficacy endpoints, RFS will not be analyzed since the current definition of DCR is same RFS. And 12-week RBC transfusion independence rates won't be provided due to clinical concerns.

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 the current version of MedDRA. 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 CTCAE Version 4.03 or customized AE severity grading as defined in the protocol Appendix B (for hemagglutination and microangiopathy AEs). 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" on the AE CRF to the question of "Relationship to magrolimab" or "Relationship to azacitidine". 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 Department 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 1 or both of the following:

- Any AEs with an onset date on or after the study drug start date and no later than 30 days after permanent discontinuation of study drug and before the first date of new anti-cancer therapy including SCT
- Any AEs leading to discontinuation of study drug.

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 30 days after the date of the last dose of study drug

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

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 by Severity

The number and percentage of subjects who experienced at least 1 TEAE will be provided and summarized by SOC, and PT. For the AE categorizes described below, summaries will be provided by SOC, PT and maximum severity:

- TEAEs
- TEAEs with Grade 3 or higher
- TE magrolimab-related AEs
- TE azacitidine-related AEs

- TE magrolimab-related AEs with Grade 3 or higher
- TE azacitidine-related AEs with Grade 3 or higher
- TE SAEs
- TE magrolimab-related SAEs
- TE azacitidine-related SAEs
- TEAEs leading to discontinuation of azacitidine
- TEAEs leading to discontinuation of magrolimab
- TE AEs leading to death (ie, outcome of death)
- TEAEs leading to dose delay or interruption of azacitidine
- TEAEs leading to dose reduction of azacitidine
- TEAEs leading to dose delay or interruption of magrolimab
- TEAEs leading to dose reduction of magrolimab

A brief, high-level summary of AEs described above will be provided by the number and percentage of subjects who experienced the above AEs.

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 for a given subject during the study.

In addition to the above summary tables, all TEAEs, TEAEs of Grade 3 or higher, TE SAEs and TE treatment-related AEs 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 AEs with Grade 3 or higher
- All SAEs
- All Deaths
- All AEs leading to death (ie, outcome of death)

- All AEs leading to discontinuation of any study drug
- TEAEs leading to dose delay or temporary interruption of any study drug
- TEAEs leading to dose reduction of any study drug

7.1.6.2. Summary of Deaths

A summary (number and percentage of subjects) of deaths will be provided. The summary will include the following categories:

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

7.1.7. Additional Analysis of Adverse Events

The incidence of infusion reaction AEs and Treatment-Emergent AEs will be examined.

7.1.7.1. Infusion Reaction Adverse Events (IRAE)

The incidence of infusion reaction AEs will be examined. Infusion reaction AEs are defined by the NCI CTCAE (under the category "General disorders and administration site conditions") as "a disorder characterized by adverse reaction to the infusion of pharmacological or biological substances". For the purpose of this study, they are defined as AEs described in Amendment 7 that occur within the 24-hour period beginning from the start of the infusion.

The number and percentage of subjects who experienced any of the infusion reaction AEs events assessed by investigators will be summarized by PT.

7.1.7.2. Treatment-Emergent Adverse Events (TEAE) of Special Interest

The following AEs of special interest (may not limit to) will be summarized:

- Anaemia (MST Anemia_Extravascular Transient Hemolysis)
- Infusion Related Reaction (IRR) (Hypersensitivity (SMQ <narrow>) – within one day of magrolimab infusion)
- Transfusion Reactions due to Magrolimab Interference with RBC typing (Gilead's MST)
- Thromboembolic Events (Embolic and Thrombotic Events (SMQ))
- Pneumonitis (Interstitial Lung Disease (SMQ))

- AE onset time within 2 weeks, >2weeks - 2 months, >2-6 months, >6-12 months, and >12 months of first dosing of any study drug

  — Anaemia/Hemolytic Anemia

  — IRR

  — Interference with Blood Cross Match or Packed RBC Transfusion Outcomes

  — Thromboembolic Events

  — Pneumonitis

  — Immune-Mediated Events

Number and percentage of subjects with AEs of Clinical significance will be summarized by PT.

7.1.7.3. Other Important Safety Topics

- Infections and Infestations (SOC)
- Immune-Mediated Events (Immune-mediate/autoimmune disorder (SMQ) - Narrow)

Number and percentage of subjects with AEs of other important safety topics (may not limit to the above list) will be summarized by PT.

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 30 days for subjects who have permanently discontinued study drug and before new anti-cancer therapy including SCT. 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 for hematology, serum chemistry, and coagulation separately. Values falling outside of the relevant reference range and/or having a severity grade of 1 or higher on CTCAE severity grade will be flagged in the data listings, as appropriate.

Scatter plots of lab parameters will include (but not limit to) hemoglobin, platelet, and absolute neutrophil counts across time will be provided.

7.2.1. Summaries of Numeric Laboratory Results

Descriptive statistics will be provided for chemistry, hematology, and coagulation as follows:

- Baseline values
- Postbaseline maximum value
- Postbaseline minimum value
- Change and percentage change from baseline to postbaseline maximum value
- Change and percentage change from baseline to postbaseline 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 study drug. Change from baseline to a postbaseline visit will be defined as the visit 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.

In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.7.3.

7.2.2. Graded Laboratory Values

CTCAE Version 4.03 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 drug plus 30 days for subjects who permanently discontinued study drug and before new anti-cancer therapy including SCT, or the last available date in the database snapshot for subjects who were still on treatment at the time of an interim analysis. 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

The following summaries (number and percentage of subjects) for laboratory abnormalities will be provided by lab test:

- Baseline grade (Grade 0 to 4 separately, Grade 3 or 4, Grade 1 to 4, and Missing)
- Worst treatment-emergent laboratory abnormalities postbaseline grade (Grade 1 to 4 separately, Grade 3 or 4, and Grade 1 to 4)

The summary of the baseline abnormalities will use the number of subjects in the Safety Analysis Set as the denominator. The summary of the worst treatment-emergent laboratory abnormalities postbaseline is the number of subjects with nonmissing postbaseline values up to 30 days after the last dosing date.

A by-subject listing of treatment-emergent Grade 3 or 4 laboratory abnormalities will be provided by subject ID number and time point 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 subjects 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

The summary will include data from all postbaseline visits up to 30 days after the last dose of study drug. For individual laboratory tests, subjects will be counted once based on the most severe postbaseline values. For both the composite endpoint of AST or ALT and total bilirubin, subjects will be counted once when the criteria are met at the same postbaseline visit date. The denominator is the number of subjects in the Safety Analysis Set who have nonmissing postbaseline values of all relevant tests at the same postbaseline visit date. A listing of subjects who met at least 1 of the above criteria will be provided.

7.2.4. Shifts Relative to the Baseline Abnormality Grade

Shift tables will be presented by showing change in abnormality grade from baseline to the worst postbaseline abnormality grade for chemistry, hematology, and coagulation.

7.3. Body Weight and Vital Signs

Descriptive statistics will be provided for body weight and vital signs as follows:

- Baseline value
- Postbaseline maximum value

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

A baseline value will be defined as the last available value collected on or prior to the date/time of first dose of study drug. Change from baseline to a postbaseline visit will be defined as the postbaseline value minus the baseline value. Body weight and vital signs measured at unscheduled visits will be included for the baseline value selection.

In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.7.3. No formal statistical testing is planned.

A by-subject listing of vital signs will be provided by subject ID number and visit in chronological order. Body weight, height and BMI will be included in the vital signs listing, if space permits. If not, they will be provided separately.

7.4. Prior and Concomitant Medications

Medications collected at screening and during the study will be coded using the current version of 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.

Prior medications will be summarized by Anatomical Therapeutic Chemical (ATC) drug class Level 2 and preferred name using the number and percentage of subjects. A subject reporting the same medication more than once will be counted only once when calculating the number and percentage of subjects who received that medication. The summary will be ordered alphabetically by ATC medical class and then by preferred term in order of descending overall frequency within each ATC medical class. For drugs with the same frequency, sorting will be done alphabetically.

For the purposes of analysis, any medication with a start date prior to the first dosing date of study drug will be included in the prior medication summary 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.

Summaries will be based on the Safety Analysis Set. No formal statistical testing is planned.

7.4.2. Concomitant Medications

Concomitant medications are defined as medications taken while a subject took study drug. Use of concomitant medications will be summarized by ATC drug class Level 2 and preferred name using the number and percentage of subjects. A subject reporting the same medication more than once will be counted only once when calculating the number and percentage of subjects who received that medication. The summary will be ordered alphabetically by ATC medical class and then by preferred term in descending overall frequency. For drugs with the same frequency, sorting will be done alphabetically.

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 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 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 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 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. Summaries will be based on the Safety Analysis Set. No formal statistical testing is planned.

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.

7.5. Electrocardiogram (ECG) Results

The QT interval (measured in millisecond [msec]) is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle. The QT interval represents electrical depolarization and repolarization of the ventricles. The QT interval is affected by heart rate, and a number of methods have been proposed to correct QT for heart rate.

Corrected QT (QTc) intervals will be derived using Fridericia's correction (QTcF) as follows:

$$QTcF = \frac{QT}{\sqrt[3]{RR}}$$

where QT is measured in msec; RR = 60/Heart Rate (beats per min [bpm]) and RR is measured in seconds

The maximum post-baseline QTcF interval values obtained during the study will be summarized within the following categories:

- > 450 msec
- > 480 msec
- > 500 msec

The maximum post-baseline change from baseline in QTcF interval values obtained during the study will also be summarized within the following categories:

- > 30 msec
- > 60 msec

The maximum post-infusion change from prior-infusion in QTcF interval values obtained during the study will also be summarized using descriptive statistics.

For the summaries of maximum post-baseline QTcF interval, maximum post-baseline change from baseline in QTcF interval, and maximum post-infusion change from pre-infusion in QTcF interval, both triplicate and one-time measurements will be included.

QTcF and uncorrected QT values at each visit and change from baseline at each visit will be summarized for the Safety Analysis Set using descriptive statistics. For baseline, as long as triplicate measurements are available prior to the first study treatment, the average of triplicate results will be defined as baseline. Otherwise, the last non-missing value of one-time measurement prior to the first study treatment is defined as baseline. At each post-treatment visit, the average of triplicate measurements takes precedence over one-time measurement value as well.

7.6. Other Safety Measures

Post treatment anti-cancer therapies (other than those allowed per-protocol) will be provided in a by-subject listing sorted by subject ID number and administration date in chronological order.

7.7. Changes from Protocol-Specified Safety Analyses

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

8. PHARMACOKINETIC (PK) ANALYSES

Individual patient's concentration data for magrolimab will be listed based on the sampling time point. Summary statistics (n, mean, median, SD, coefficient of variation [%CV], min, max, Q1, Q3, and geometric mean) will be presented for magrolimab serum concentrations at each scheduled time point, split by dosing groups in each cohort. Descriptive graphical plots of individual and mean (SD) concentration-versus-time profiles split by dosing groups in each cohort will be generated.

Missing concentration values will be reported as is in data listings. Concentration values below lower limit of quantitation will be set to zero in summary statistics, and reported as-is in data listings.

PK data from this study will be combined with data from other studies and analyzed using a population PK methodology, but that will be reported separately. CCI [redacted]

9. IMMUNOGENICITY ANALYSES

The immunogenicity analyses will use the Immunogenicity Analyses Set. The following measures of anti magrolimab antibody positivity will be reported: ADA prevalence, ADA incidence (i.e. sum of Treatment-Induced and Treatment-Boosted ADA rate), ADA transience/persistence rate, and neutralizing anti-body (nAb) incidence.

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

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

Treatment-Induced ADA Rate: the proportion of subjects who had negative baseline ADA sample and at least one positive post-treatment ADA sample based on subjects 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 subjects 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

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 subjects 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 subjects who had transient ADA is based on the subjects evaluable for ADA incidence.

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

If relevant, CCI tabular or graphical analysis may be conducted to determine the relationship between immunogenicity assay positivity and 1 or more safety, PK, or efficacy parameters (for example, drug concentrations, AEs, CR rate, DOR). Mixed effects modeling may also be conducted to evaluate these relationships, but that will be reported separately. The rate of neutralizing antibody positive subjects will also be summarized.

10. REFERENCES

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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
06 FEB 2023	Global	Include AML efficacy analyses	To serve primary and final CSR analyses
06 FEB 2023	Global	Include all cohorts	To serve primary and final CSR analyses

13. APPENDICES

Appendix 1. Response Criteria in MDS (IWG 2006 Criteria)

Category	Response Criteria (responses must last ≥ 4 weeks)
Complete Remission	Bone marrow ≤ 5% myeloblasts with normal maturation of all cell lines[a] Persistent dysplasia will be noted[a,b] Peripheral blood[c] • Hgb ≥ 11 g/dL • Platelets ≥ 100 × 10^9/L • Neutrophils ≥ 1.0 × 10^9/L[b] • Blasts 0%
Partial Remission	All CR criteria if abnormal before treatment except: • Bone marrow blasts decreased by ≥ 50% over pretreatment but still > 5% • Cellularity and morphology not relevant
Marrow CR[b]	• Bone marrow ≤ 5% myeloblasts and decrease by ≥ 50% over pretreatment[b] • Peripheral blood: if HI responses, they will be noted in addition to marrow CR[b]
Stable Disease	• Failure to achieve at least PR, but no evidence of progression for > 8 weeks
Failure	Death during treatment or disease progression characterized by worsening cytopenias, increase in percentage of bone marrow blasts, or progression to a more advanced MDS FAB subtype than pretreatment
Relapse after CR or PR	At least 1 of the following: • Return to pretreatment bone marrow blast percentage • Decrement of ≥ 50% from maximum remission/response levels in granulocytes or platelets • Reduction in Hgb concentration by ≥ 1.5 g/dL or transfusion dependence[d]
Cytogenetic Response	• Complete: Disappearance of chromosomal abnormality without appearance of new ones • Partial: At least 50% reduction of the chromosomal abnormality
Disease Progression	For patients with: • Less than 5% blasts: ≥ 50 increase in blasts to > 5% blasts • 5%-10% blasts: ≥ 50% increase in blasts to > 10% blasts • 10%-20% blasts: ≥ 50% increase in blasts to > 20% blasts • 20%-30% blasts: ≥ 50% increase in blasts to > 30% blasts Any of the following: • At least 50% decrement from maximum remission/response in granulocytes or platelets • Reduction in Hgb by ≥ 2 g/dL[d] • Transfusion dependence[d]

Source: {Cheson 2006}
Abbreviations: CR = complete remission; FAB = myelodysplastic syndrome French-American-British classification; Hgb = hemoglobin; IWG = International Working Group; MDS = myelodysplastic syndrome; PR = partial remission.

a. Dysplastic changes should consider the normal range of dysplastic changes
b. Modification to IWG response criteria
c. In some circumstances, protocol therapy may require the initiation of further treatment (e.g., consolidation, maintenance) before the 4-week period. Such patients can be included in the response category into which they fit at the time the therapy is started. Transient cytopenias during repeated chemotherapy courses should not be considered as interrupting durability of response, as long as they recover to the improved counts of the previous course.
d. Impact of anemia must be deemed disease-related and not due to study treatment.

Appendix 2. Response Criteria in AML (ELN 2017 Recommendations)

Response Criteria	Definitions			
	Neutrophils	Platelets	Bone Marrow Blasts	Other
Complete Remission without minimal residual disease (CR_{MRD-})	$\geq 1.0 \times 10^9$/L	$\geq 100 \times 10^9$/L	< 5%	If studied pretreatment, CR with negativity for a genetic marker by real-time quantitative polymerase chain reaction (RT-qPCR) or similar modality or CR with negativity by multi-color flow cytometry
Complete Remission (CR)	$\geq 1.0 \times 10^9$/L	$\geq 100 \times 10^9$/L	< 5%	Absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; MRD positive or unknown
Complete Remission with Incomplete Hematologic Recovery (CRi)	Neutrophils $\geq 1.0 \times 10^9$/L or Platelets $\geq 100 \times 10^9$/L		< 5%	Absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; MRD positive or unknown (All CR criteria except residual neutropenia [$< 1.0 \times 10^9$/L] or thrombocytopenia [$< 100 \times 10^9$/L])
Morphologic Leukemia-Free State (MLFS)			< 5%	Absence of blasts with Auer rods; absence of extramedullary disease; no hematologic recovery required; marrow should not merely be "aplastic"; at least 200 cells should be enumerated or cellularity should be at least 10%
Partial Remission (PR)	$\geq 1.0 \times 10^9$/L	$\geq 100 \times 10^9$/L	Decrease of bone marrow blast percentage to 5% to 25%; and decrease of pretreatment bone marrow blast percentage by at least 50%	Blasts < 5% with Auer rods may also be considered a PR
Stable Disease (SD)	Absence of CR_{MRD-}, CR, CRi, PR, MLFS; and criteria for progressive disease not met			
Progressive Disease (PD)	• Evidence for an increase in bone marrow blast percentage and/or increase of absolute blast counts in the blood: ○ 50% increase in marrow blasts over baseline (a minimum 15% point increase is required in cases with < 30% blasts at baseline; or persistent marrow blast percentage of > 70% over at least 3 months; without at least a 100% improvement in ANC to an absolute level ($> 0.5 \times 10^9$/L [500/µL]), and/or platelet count to $> 50 \times 10^9$/L (50,000/µL) non-transfused]; or ○ 50% increase in peripheral blasts (WBC × % blasts) to $> 25 \times 10^9$/L (> 25,000/µL) (in the absence of differentiation syndrome); or • New extramedullary disease			

Source: {Dohner 2017}
Abbreviations: AML = acute myeloid leukemia; ANC = absolute neutrophil count; CR = complete remission; MRD = minimal residual disease; WBC = white blood cell count.

Appendix 3. Additional Response Definitions Used in This Trial (2003 IWG Criteria)

Response Criteria	Definitions			
	Neutrophils	Platelets	Bone Marrow Blasts	Other
Cytogenetic CR (cCR)	$\geq 1.0 \times 10^9$/L	$\geq 100 \times 10^9$/L	< 5%	Cytogenetics normal and no evidence of extramedullary disease
Molecular CR (mCR)	$\geq 1.0 \times 10^9$/L	$\geq 100 \times 10^9$/L	< 5%	Molecular investigations normal and no evidence of extramedullary disease
Treatment Failure[a]	Lack of response/Progressive Disease + loss of clinical benefit			

Source: {Cheson 2003}
Abbreviations: IWG = International Working Group.
a. Treatment failure defined for this protocol

5F9005-SAP-Prot9-V3

ELECTRONIC SIGNATURES

Signed by	Meaning of Signature	Server Date (dd-MMM-yyyy hh:mm:ss)
PPD	Clinical eSigned	PPD
PPD	Biostatistics eSigned	1PPD