STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 2, Multi-Arm Study of Magrolimab in Patients With Solid Tumors
Plain Language Short Title:	Study of Magrolimab in Patients With Solid Tumors
Name of Test Drug:	Magrolimab (GS-4721)
Study Number:	GS-US-548-5918
Protocol Version (Date):	Amendment 5 (24 October 2023)
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Analysis Plan Author(s):	PPD

CONFIDENTIAL AND PROPRIETARY INFORMATION

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ADA	anti-drug antibody
AE	adverse event
AECI	adverse events of clinical importance
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate transaminase
ATC	Anatomical Therapeutic Chemical
BMI	body mass index
BOR	best overall response
BSA	body surface area
CBR	clinical benefit rate
CI	confidence interval
CR	complete response
CRF	case report form
CSR	clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
DOR	duration of response
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
EOT	end of treatment
KM	Kaplan-Meier
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified intent to treat
NA	not applicable
NCI	National Cancer Institute
NE	not evaluable
NTLs	non-target lesions
ORR	objective response rate
OS	overall survival
PD	disease progression
PFS	progression-free survival
PK	pharmacokinetics
PR	partial response
PT	preferred term
Q1, Q3	first quartile, third quartile
RECIST	Response Evaluation Criteria in Solid Tumors (version 1.1)
SAE	serious adverse event
SAP	statistical analysis plan

SD	stable disease
SE	standard error
SMQ	Standard MedDRA Query
StD	standard deviation
SOC	system organ class
TLs	target lesions
ULN	upper limit of normal
WHO	World Health Organization

1. INTRODUCTION

This statistical analysis plan (SAP) describes the statistical analysis methods and defines key elements including variable definitions for analysis of data of Study GS-US-548-5918 in support of the clinical study report (CSR). This SAP is based on the study protocol amendment 5.0 dated 24 October 2023. 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 and Endpoints

Primary Objectives	Primary Endpoints
• To evaluate the safety, tolerability, and recommended Phase 2 dose of magrolimab + docetaxel combination therapy in solid tumors (Safety Run-in Cohort 1, Phase 2 Cohorts 1a, 1b, and 1c) • To evaluate the efficacy of magrolimab + docetaxel combination therapy in solid tumors as determined by investigator-assessed objective response rate (ORR) (Phase 2 Cohorts 1a, 1b, and 1c)	• Incidence of adverse events (AEs) and laboratory abnormalities according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE), Version 5.0 (Safety Run-in Cohort 1, Phase 2 Cohorts 1a, 1b, and 1c) • ORR, defined as the proportion of patients who achieve a complete response or partial response, as measured by Response Evaluation Criteria in Solid Tumors (RECIST), Version 1.1, as determined by investigator assessment (Phase 2 Cohorts 1a, 1b, and 1c)
Secondary Objectives	**Secondary Endpoints**
• To evaluate progression-free survival (PFS) by investigator assessment (Phase 2 Cohorts 1a, 1b, and 1c) • To evaluate additional measures of efficacy of magrolimab + docetaxel combination therapy, including duration of response (DOR) and overall survival (OS) (Phase 2 Cohorts 1a, 1b, and 1c) • To evaluate the pharmacokinetics (PK) and immunogenicity of magrolimab when given with docetaxel as a combination therapy (Safety Run-in Cohort 1, Phase 2 Cohorts 1a, 1b, and 1c)	• PFS from date of dose initiation as determined by investigator assessment per RECIST, Version 1.1 (Phase 2 Cohorts 1a, 1b, and 1c) • DOR, defined as time from first documentation of complete response or partial response to the earliest date of documented disease progression, per RECIST, Version 1.1, or death from any cause, whichever occurs first, as determined by investigator assessment (Phase 2 Cohorts 1a, 1b, and 1c) • OS, defined as date of dose initiation (Phase 2 Cohorts 1a, 1b, and 1c) to death from any cause. • Magrolimab concentration versus time and antidrug antibodies to magrolimab (Safety Run-in Cohort 1; Phase 2 Cohorts 1a, 1b, and 1c)

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1.2. Study Design

1.2.1. Study Design

This Phase 2, open-label, multicenter, multi-arm study is evaluating magrolimab + docetaxel combination therapy for patients with solid tumors. This study will consist of the following Safety Run-in Cohort:

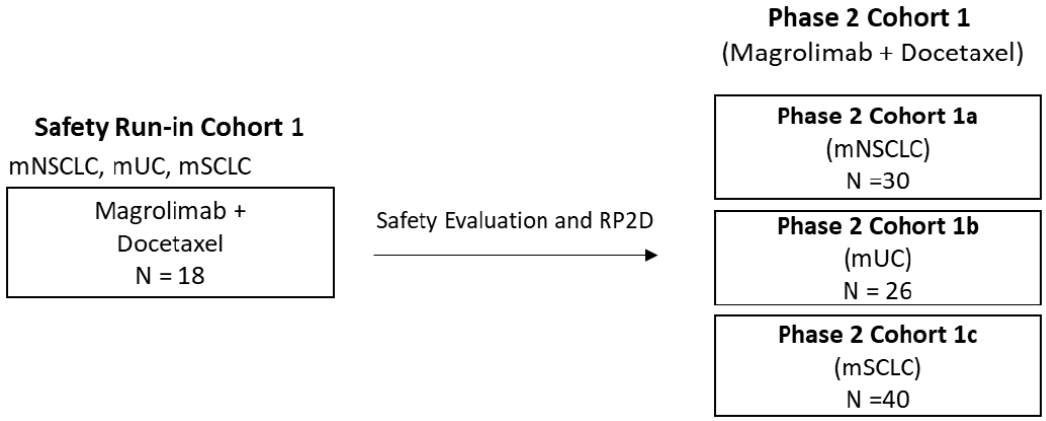
- **Safety Run-in Cohort 1:** magrolimab + docetaxel combination in patients with solid tumors (mNSCLC, mUC, and mSCLC)

After completion of Safety Run-in Cohort 1, Phase 2 Cohort 1 will occur with Cohort 1a, 1b, and 1c for mNSCLC, mUC, and mSCLC, respectively.

Up to approximately 114 patients may be enrolled in the study, with up to approximately 18 patients in Safety Run-in Cohort 1 and 96 patients in Phase 2 Cohort 1.

The study schematic is presented in Figure 1-1.

Figure 1-1. Study Schema



mNSCLC = metastatic non-small cell lung cancer; mSCLC = metastatic small cell lung cancer; mUC = metastatic urothelial cancer; RP2D = recommended Phase 2 dose

1.2.2. Safety Run-in Cohort 1

A dose-limiting toxicity (DLT) evaluation period of 1 cycle (21 days) will occur. After 6 patients have completed the DLT evaluation period, decision will be made on further expansion or dose de-escalation.

Even though no dose-dependent toxicities have been observed with magrolimab, in order to preserve the efficacious doses of the combination partner drugs, dose de-escalation will take place for magrolimab.

Dose de-escalation decisions will be made as follows:

- If 2 or fewer of 6 DLT-evaluable patients experience a DLT in Cycle 1, enrollment into Phase 2 Cohort 1 will begin at this dose level as the recommended Phase 2 dose.

- If more than 2 patients experience at least 1 DLT during Cycle 1, enrollment at the current dose level will immediately stop and dose de-escalation will occur. Up to another 6 patients will then be enrolled and evaluated at a lower dose level in the same manner.

1.2.3. Phase 2 Cohort 1

Once Safety Run-in Cohort 1 is completed and the recommended dose for Phase 2 Cohort 1 is determined, the sponsor will open Phase 2 Cohort 1. Phase 2 Cohort 1 will treat up to 30 patients with mNSCLC (Phase 2 Cohort 1a), up to 26 patients with mUC (Phase 2 Cohort 1b), and up to 40 patients with mSCLC (Phase 2 Cohort 1c) to evaluate efficacy.

1.2.4. Study Treatments

Table 1-1 shows the study treatments for Safety Run-in Cohort 1 and 1-2 shows the study treatments for Phase 2 Cohort 1.

Table 1-1. Safety Run-in Cohort 1: Dose Level, Schedule, and De-escalation

Drug	Dose Level	Dosing (Cycles Are 21 Days)		
		Cycle 1	Cycle 2	Cycle 3+ (maintenance dosing)
Magrolimab	Starting dose 30 mg/kg	1 mg/kg IV (3 h ± 30 min) on Day 1 (priming dose), 30 mg/kg IV (2 h ± 30 min) on Days 8 and 15	30 mg/kg IV (2 h ± 30 min) on Days 1, 8, and 15	60 mg/kg IV (2 h ± 30 min) on Day 1
	De-escalation Level −1 20 mg/kg	1 mg/kg IV (3 h ± 30 min) on Day 1 (priming dose); 20 mg/kg IV (2 h ± 30 min) on Days 8 and 15	20 mg/kg IV (2 h ± 30 min) on Days 1, 8, and 15	45 mg/kg IV (2 h ± 30 min) on Day 1
	De-escalation Level −2 15 mg/kg	1 mg/kg IV (3 h ± 30 min) on Day 1 (priming dose); 15 mg/kg IV (2 h ± 30 min) on Days 8 and 15	15 mg/kg IV (2 h ± 30 min) on Days 1, 8, and 15	30 mg/kg IV (2 h ± 30 min) on Day 1
Docetaxel	75 mg/m^2	75 mg/m^2 IV (1 h ± 5 min) on Day 1	75 mg/m^2 IV (1 h ± 5 min) on Day 1	75 mg/m^2 IV (1 h ± 5 min) on Day 1

IV = intravenous

Table 1-2. Phase 2 Cohort 1: Dose Level and Schedule

Drug	RP2D[a] Starting Dose	Dosing (Cycles Are 21 Days)		
		Cycle 1	Cycle 2	Cycle 3+ (maintenance dosing)
Magrolimab	30 mg/kg	1 mg/kg IV (3 h ± 30 min) on Day 1 (priming dose); 30 mg/kg IV (2 h ± 30 min) on Days 8 and 15	30 mg/kg IV (2 h ± 30 min) on Days 1, 8, and 15	60 mg/kg IV (2 h ± 30 min) on Day 1
	OR 20 mg/kg	1 mg/kg IV (3 h ± 30 min) on Day 1 (priming dose); 20 mg/kg IV (2 h ± 30 min) on Days 8 and 15	20 mg/kg IV (2 h ± 30 min) on Days 1, 8, and 15	45 mg/kg IV (2 h ± 30 min) on Day 1
	OR 15 mg/kg	1 mg/kg IV (3 h ± 30 min) on Day 1 (priming dose); 15 mg/kg IV (2 h ± 30 min) on Days 8 and 15	15 mg/kg IV (2 h ± 30 min) on Days 1, 8, and 15	30 mg/kg IV (2 h ± 30 min) on Day 1
Docetaxel	75 mg/m^2 IV	75 mg/m^2 IV (1 h ± 5 min) on Day 1	75 mg/m^2 IV (1 h ± 5 min) on Day 1	75 mg/m^2 IV (1 h ± 5 min) on Day 1

IV = intravenous; RP2D = recommended Phase 2 dose
a RP2D as determined in Safety Run-in Cohort 1.

1.3. Sample Size and Power

Table 1-3 presents the sample size calculations. For Phase 2 Cohort 1, a sample size of 30 patients in the mNSCLC cohort and 40 patients for the mSCLC cohort were calculated using one sample proportion test. The sample size of 26 patients for the mUC cohort was calculated using exact method instead of one sample test due to smaller sample size.

Table 1-3. Sample Size Calculations

Tumor Type	Sample Size	Null ORR	Alternative ORR	1-sided alpha	Power
mNSCLC	30	13%	25%	0.2	81%
mUC	26	12.4%	28%	0.1	78%
mSCLC	40	9%	20%	0.15	84%

mNSCLC = metastatic non-small cell lung cancer; mSCLC = metastatic small cell lung cancer; mUC = metastatic urothelial cancer; ORR = objective response rate

The null ORR for each of the respective tumor cohorts are based on historical taxane efficacy data in the second line setting {Bellmunt 2017, Rittmeyer 2017, Smit 1998}. Power calculations were performed using EAST 6.5 and nQuery 8.0.

2. TYPE OF ANALYSIS

2.1. Dose Determination Analysis

For the purposes of making any dose de-escalation decisions for Safety Run-in Cohort 1, dose determination analyses of relevant safety data focusing on DLTs and overall safety profile was conducted by the sponsor after all patients had completed required dosing cycles (21 days) and the follow-up period as defined in Section 1.2.2. Dose Determination Analyses has been completed and is not within the scope of this SAP.

2.2. Informal Interim Analyses

No formal interim efficacy analysis, which may lead to early termination for efficacy or futility, is planned.

For the purpose of potential Phase 3 planning, informal interim analyses may be conducted per cohort after at least 20 patients enrolled in each tumor type (i.e., including applicable patients from the combined Safety Run-in) and have been followed up for approximately 19 weeks.

2.3. Primary Analysis

For each of the subcohorts in Phase 2 Cohort 1, the primary analysis of ORR will be conducted approximately 6 months after the last patient is enrolled, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized for the analysis.

2.4. Final Analysis

The final analysis may be performed after all patients have completed the study or discontinued early, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized.

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.

3.1. Analysis Sets

For each analysis set, the number and percentage of patients eligible for inclusion, as well as the number and percentage of patients who were excluded and the reasons for their exclusion, will be summarized by cohort (Safety run-in cohort 1, Phase 2 cohort 1a, 1b, 1c, respectively).

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

3.1.1. All Enrolled Analysis Set

All Enrolled Analysis Set includes all patients who received a study subject identification number in the study after screening.

3.1.2. Modified ITT Analysis Set

The modified ITT Analysis Set (mITT) includes all enrolled patients who took at least 1 dose of any study drug. This is the primary analysis set for efficacy analyses of Phase 2 Cohort 1a, 1b and 1c, respectively.

3.1.3. Safety Analysis Set

The Safety Analysis Set includes all patients who took at least 1 dose of any study drug. This is the primary analysis set for safety analysis (except for DLTs) of both Safety Run-in Cohort 1 and Phase 2 Cohort 1a, 1b, 1c, respectively.

3.1.4. Dose-Limiting Toxicity (DLT) Evaluable Analysis Set

For Safety Run-in Cohort 1, the primary analysis set for the primary DLT analysis is the DLT Evaluable Analysis Set, defined as all patients who meet 1 of the following criteria in the DLT evaluable period (defined as 21 days of the first dosing cycle):

- The patient experienced a DLT at any time after initiation of the first infusion of magrolimab.
- The patient did not experience a DLT and completed at least 2 infusions of magrolimab (21-day cycle) and at least 1 dose of docetaxel in Safety Run-in Cohort 1.

For the 2nd criteria above, the 2 doses of magrolimab and 1 dose of docetaxel are infused within the 21-day cycle and patient is on study for at least 21 days after the first dose in Safety Run-in Cohort 1.

3.1.5. Pharmacokinetic Analysis Set

The PK analysis will be conducted on the PK Analysis Set, defined as all patients who received any amount of magrolimab and have at least 1 measurable posttreatment serum concentration of magrolimab.

3.1.6. Immunogenicity Analysis Set

The immunogenicity analysis will be conducted on the Immunogenicity Analysis Set, defined as all patients who received any amount of magrolimab and have at least 1 evaluable anti-magrolimab antibody test result.

3.1.7. Biomarker Analysis Set

The biomarker analysis will be conducted on the Biomarker Analysis Set, defined as all patients who received any study drug and have at least 1 evaluable biomarker measurement available.

3.2. Subject Grouping

For primary analyses and final analysis based on the mITT or Safety Analysis Set, patients will be grouped according to the cohort they were enrolled in: Safety Run-in Cohort 1, Phase 2 Cohort 1a (mNSCLC), Phase 2 cohort 1b (mUC), and Phase 2 cohort 1c (mSCLC).

For informal interim analysis based on the mITT or Safety Analysis Set, patients will be grouped according to the tumor type at enrollment as follows:

- Safety Run-in cohort 1 with tumor type mNSCLC + Phase 2 cohort 1a (mNSCLC)
- Safety Run-in cohort 1 with tumor type mUC + Phase 2 cohort 1b (mUC)
- Safety Run-in cohort 1 with tumor type mSCLC + Phase 2 cohort 1c (mSCLC)

Here the tumor type from safety run-in cohort 1 is determined by the type of cancer from medical history as collected in CRF.

3.3. Strata and Covariates

This study does not have randomization so no randomization strata is defined.

No covariates will be included in efficacy and safety analyses.

3.4. Examination of Subject Subgroups

There are no prespecified patient subgroupings for efficacy and safety analyses.

3.5. Adjustment for Multiplicity

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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.

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 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 Study Day 1 (in years) will be used for analyses and presented in listings. If age at Day 1 is not available for a subject, then age derived based on date of birth and the date of Study Day 1 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 screen failures or patients who are not enrolled, 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 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 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, respectively).

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.

PK Data Handling

Natural logarithmic transformation will be used for analyzing non-BLQ concentrations and PK parameters. Concentration values that are below the limit of quantitation (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. The number of samples will be summarized to reflect the actual number of samples assessed at that time point.

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 participants 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 participant has a concentration value of BLQ for the time point, the minimum value will be displayed as "BLQ."
- If more than 25% of the participants 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 participants 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 participants 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 participants 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."

PK parameters that are BLQ will be excluded before log transformation or statistical model fitting and displayed as described above.

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 date of the first dose of magrolimab or the combination drug, whichever occurs first 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 enrolled but not dosed, the enrollment 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 lab assessments are provided in Table 3-1. Post-infusion lab assessments for hemoglobin and hematocrit will use nominal visit and will be excluded when applying Table 3-1. Analyses windows will be applied to summary tables of lab results by visits and change from baseline if applicable.

Table 3-1. Analysis Visit Windows for Lab By-visit Summaries

Analysis Visit	Nominal Study Day	Visit Window Study Day	
		Lower Limit	Upper Limit
Baseline		(none)	1[a]
Day 2[b]	2	1[c]	2
Week 1	8	3	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	53
Week 9	64	54	74
Week xx[d]	(xx)*7 + 1	(xx)*7 - 9	(xx)*7 + 11

a Prior to first dose date time
b Day 2 visit not applicable to chemistry lab assessments. Chemistry labs assessed post first dose date time through study day 2 will be assigned to "Week 1" visit
c Post first dose date time
d xx >= 12

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 average of the measurements for continuous data, or the measurement with the worst 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 average will be taken for continuous data and the worst severity will be taken for categorical data, unless otherwise specified.

3.9. Assessment of COVID-19 Impact

This study was ongoing during the novel coronavirus (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. The following special situations due to COVID-19 may be handled in the analysis:

- Study treatment or study discontinuation due to COVID-19

- Protocol deviations due to COVID-19

- Adverse events due to COVID-19

- Death due to COVID-19

4. PROTOCOL DEVIATIONS

Patients who did not meet at least one eligibility criterion for study entry, but enrolled in the study will be summarized by cohort regardless of whether they were exempted by the sponsor or not, based on the All Enrolled Analysis Set. The summary will also present the number and percentage of patients who did not meet specific criteria.

Protocol deviations occurring after patients entered the study are documented during routine monitoring. The number and percentage of patients with important protocol deviations by deviation reason (e.g., eligibility criteria, informed consent) will be summarized by cohort for the All Enrolled Analysis Set.

5. SUBJECT INFORMATION

In general, disposition tables and all listings will be based on All Enrolled Analysis Set. Summary of treatment exposure, prior and concomitant medications and post treatment anti-cancer therapy will be based on Safety Analysis Set. All other table summaries in this section will be based on mITT Analysis Set, unless specified otherwise.

5.1. Patient Enrollment and Disposition

Key study dates (i.e., first patient screened, first patient enrolled, last patient enrolled, last patient last visit for the primary endpoint, and last patient last visit for the clinical study report) will be provided.

A summary of patient enrollment will be provided by cohort for each country, investigator and overall.

A summary of patient disposition will be provided by cohort. This summary will present the number of patients who met all eligibility criteria but were not enrolled with reasons patients not enrolled, the number of patients enrolled, and the number of patients in each of the categories listed below:

- mITT Analysis Set
- Safety Analysis Set
- Continuing study treatment (magrolimab, docetaxel)
- Discontinued study drug with reasons for discontinuation of study drug (magrolimab, docetaxel)
- On-going in study
- Discontinued the study with reasons for discontinuation of study

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 All Enrolled Analyses Set corresponding to that column.

The following by-patient listings 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

5.2. Extent of Study Treatment Exposure

Extent of exposure to study treatment will be summarized using descriptive statistics for total duration of exposure, total number of infusions received, total number of cycles received for each study drug, total cumulative dose administered for each study drug, relative dose intensity (%) of each study drug, and number (%) of patients with dose modifications (i.e., infusion interruption, dose delayed or not administered) and reasons for each study drug (Magrolimab and Docetaxel) by cohort.

5.2.1. Duration of Exposure

Total duration of exposure to each study drug (Magrolimab and Docetaxel) 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 (e.g., 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, 3 weeks, 6 weeks, 9 weeks, 18 weeks, and 27 weeks, etc.

5.2.2. Relative Dose Intensity

Relative dose intensity (RDI) 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 patient's actual on-treatment period based on the study drug regimen.

Summary of relative dose intensity of magrolimab will be expressed as a percentage using the following formula:

$$Relative\ dose\ intensity\ (\%) = \left(\frac{Cumulative\ dosage\ received\ \left({}^{mg}/_{kg}\right)}{Total\ planned\ dosage\ of\ specific\ drug\left({}^{mg}/_{kg}\right)} \right) \times 100$$

Cumulative dosage (mg/kg for Magrolimab or mg/m2 for Docetaxel) received for each subject is defined as the sum of all delivered dosages of all infusions the subject received. Delivered dosage will be calculated by the actual dose received (mg) as collected in CRF devided by the subjects's weight (for Magrolimab) or BSA (for Docetaxel) collected on or before that visit.

Total assigned dosage (mg/kg or mg/m2) for each subject is defined as the sum of the assigned dosage per protocol specified dose level and dosing schedule.

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 cohort for the Safety Analysis Set.

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

5.3. Demographics and Baseline characteristics

Subject demographic variables (i.e., age, sex at birth, race, ethnicity) and baseline characteristics include but are not limited to: body weight [in kg], height [in cm], body mass index [BMI; in kg/m2], Body Surface Area [BSA; in m2], type of cancer (Bladder, Non small cell lung, Small cell lung carcinoma) and disease stage at screening, Best response of the last prior anti-cancer therapy in metastatic setting before enrollment, and ECOG performance status, will be summarized using descriptive statistics for continuous variables and using number and percentage of patients for categorical variables. This analysis will be summarized with descriptive statistics by cohort for the mITT Analysis Set.

By-patient demographic and baseline characteristic listings, including the informed consent date, will be provided.

5.4. Medical History

General medical history data will be collected at screening and will be coded using the current version of Medical Dictionary for Regulatory Activities (MedDRA).

A by-patient listing including all the information collected in the medical history eCRF and the coded terms including SOC and PT will be provided.

5.5. 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.

5.5.1. Prior Medications

Prior medications are defined as any medications taken before a patient took the first study drug.

Prior medications will be summarized by Anatomical Therapeutic Chemical (ATC) drug class Level 2 preferred name using the number and percentage of subjects by cohort and treatment group. 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 and a by-patient listing will be provided.

5.5.2. Concomitant Medications

Concomitant medications are defined as medications taken while a patient took study treatment. Use of concomitant medications will be summarized by Anatomical Therapeutic Chemical (ATC) drug class Level 2 and preferred name using the number and percentage of patients for each cohort. A patient reporting the same medication more than once within each ATC drug class will be counted only once when calculating the number and percentage of patients who received that medication. Medications may appear under multiple ATC drug classes. The summary will be ordered alphabetically by ATC medical class and then by preferred term in 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 medications with a start date prior to or on the first dosing date of study treatment and continued to be taken after the first dosing date, or started after the first dosing date but prior to or on the 30 days after last dosing date of study treatment 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 treatment will also be considered concomitant. Medications with a stop date prior to the date of first dosing date of study treatment or a start date after the last dosing date of study treatment plus 30 days will be excluded from the concomitant medication summary. Medications with partially or completely missing start and stop dates will be included in the concomitant medication summary, unless the partial missing date suggested otherwise.

Summaries will be based on the Safety Analysis Set.

All concomitant medications will be provided in a by-patient listing sorted by subject ID number and administration date in chronological order.

5.6. Prior Anti-cancer Therapy

Prior anti-cancer therapy will be coded using the World Health Organization (WHO) Drug Dictionary and summarized by Preferred Drug Name. The number of prior regimans of anti-cancer therapies in metastatic setting, therapy settings (neoadjuvant, adjuvant or metastatic), best response of the last prior anti-cancer therapy in metastatic setting before enrollment, and time from last disease progression to enrollment date will be summarized by cohort.

A by-patient listing will be provided.

5.7. On Study or Post Study Anti-cancer Therapies

All subsequent anti-cancer therapies including flag for on-study and post study anti-cancer therapies as collected in CRF will be provided in a by-patient listing sorted by patient ID number and administration date in chronological order. Note that anti-cancer therapy is not allowed during the study drug treatment per protocol, which may be violated and lead to important protocol deviation. The analysis will be performed for Safety Analysis Set.

5.8. Prior and On Study Radiation Therapy

A by-patient listing including information collected in eCRF and the flag for prior and on study radiation therapy will be provided.

5.9. Prior and On Study Surgeries and Procedures

A by-patient listing including information collected in eCRF and the flag for prior and on study surgery and procedure will be provided.

6. EFFICACY ANALYSES

In general, summary of efficacy endpoints in this section will be based on mITT Analyses Set for each of the phase 2 cohort 1a, 1b and 1c, unless specified otherwise. Listing will be based on All Enrolled Analysis Set. Safety run-in cohort 1 subjects will only be listed for efficacy related endpoints.

6.1. Primary Efficacy Endpoints

6.1.1. Definition of the Primary Efficacy Endpoints

The primary efficacy endpoint of this study is objective response rate (ORR) defined as the proportion of patients who achieve the best overall response of complete response (CR) or partial response (PR) that is confirmed at least 4 weeks after initial documentation of response. The responses are measured by response evaluation criteria in solid tumors (RECIST), Version 1.1, as determined by investigator assessment (Phase 2 cohorts 1a, 1b, and 1c). Tumor response assessments after the date of patients receiving new anticancer therapy will be excluded from the analysis. Patients who do not have baseline or on-study response status assessment, or who received subsequent anticancer therapy prior to achieving CR or PR, will be considered as non-responders.

6.1.2. Analysis of the Primary Efficacy Endpoint

For each of Phase 2 cohorts 1a, 1b and 1c, the primary analysis of ORR will be conducted approximately 6 months after the last patient is enrolled. ORR along with the 2-sided 95% exact confidence interval (CI) of ORR based on Clopper-Pearson method will be provided for each cohort.

6.1.3. Sensitivity Analysis of the Primary Efficacy Endpoint

There is no sensitivity analysis is planned.

6.2. Secondary Efficacy Endpoints

6.2.1. Definition of Secondary Efficacy Endpoints

Progression-Free Survival (PFS)

PFS is defined as the interval from the first dosing date of any study drug to the earlier date of the first documentation of objective disease progression by investigator assessment per RECIST, Version 1.1, or death from any cause.

Duration of Response (DOR)

DOR is defined for confirmed responders as duration of time from the date of initial response (first confirmed CR or PR) to the date of first documentation of disease progression per RECIST, Version 1.1, or the date of death due to any cause, whichever occurs first.

DOR = Date of disease progression/death or censoring – Date of first confirmed CR/PR + 1.

Date of initial response is the date of first response achieved and then confirmed by a subsequent disease assessment conducted prior to or at the initiation of the next line of subsequent anticancer therapy.

Date of disease progression (PD) used to calculate DOR is the first PD date prior to or on the date of initiation of subsequent anticancer therapy.

Overall Survival (OS)

OS is defined as the interval from first dosing date of any study drug to death from any cause. For patients who were not known to have died at the time of the analysis, OS data will be censored at the last date that they were known to be alive. In the event that the patient has withdrawn consent, the vital status of the patient can be obtained by site personnel from publicly available resources under applicable local laws.

6.2.2. Analysis Methods for Secondary Efficacy Endpoints

Analysis of PFS, OS and DOR (confirmed responders only) will be performed using the Kaplan-Meier method for the mITT Analysis Set. Medians, Q1, Q3, and the proportion of patients who are progression-free (for PFS only) will be provided along with corresponding 95% CIs calculated by the Brookmeyer and Crowley method with log-log transformation for each of the Phase 2 cohorts. Kaplan-Meier curves will be provided by each of the Phase 2 cohorts. Censoring rules for PFS and DOR are listed in Table 6-1.

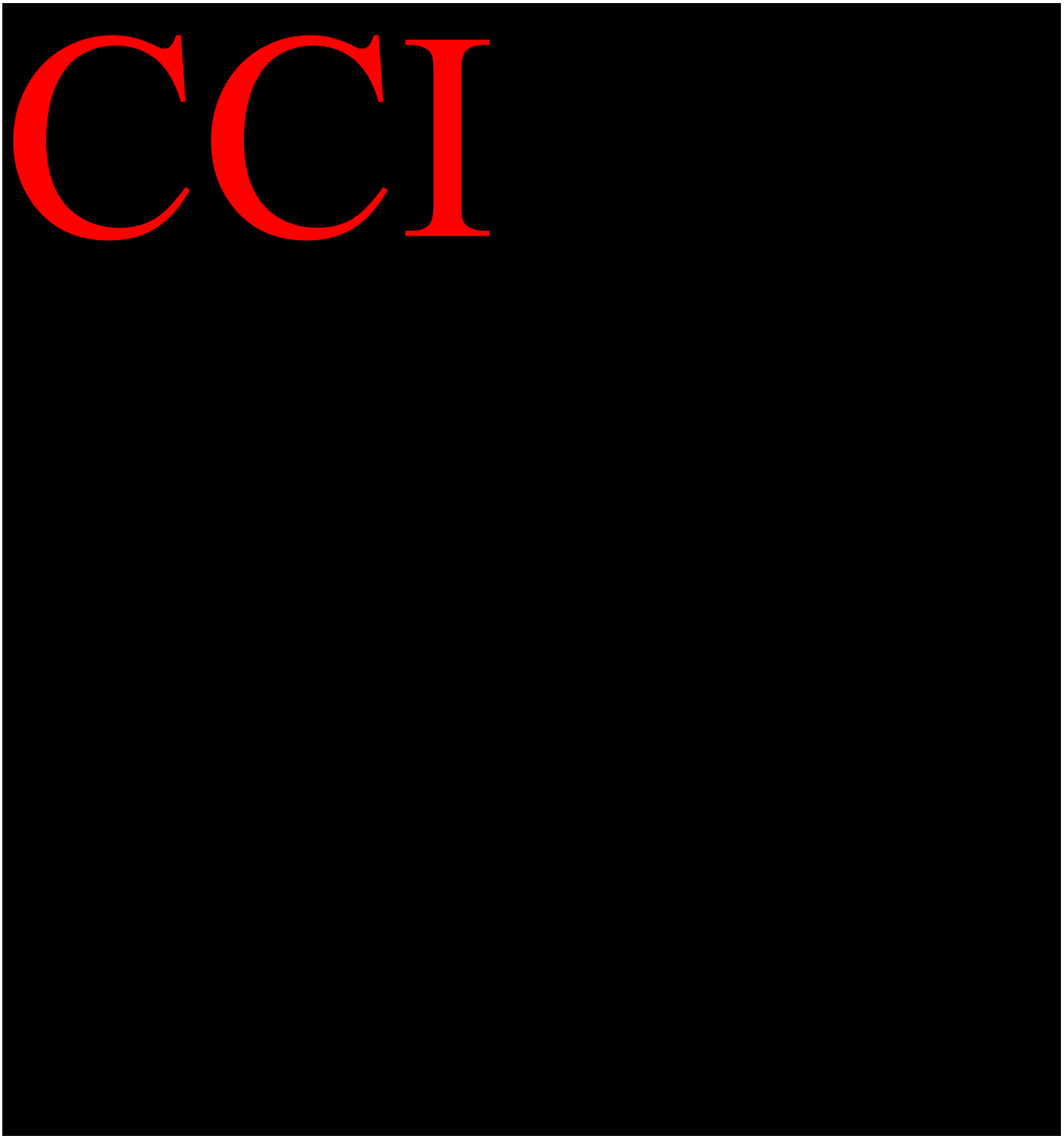
Table 6-1. Censoring rules for analysis of PFS and DOR

Situation	Censoring Rule for Analysis
Documented Progressive Disease (PD)	Progressed at date of earliest sign of PD
Death before first PD	Progressed at date of death
Death within 2 disease assessments window	Progressed at date of death
Alive and progression-free	Censored at date of last evaluable disease assessment
No PD or death before or on the initiation date of subsequent anticancer therapy	Censored at date of last evaluable assessment on or prior to subsequent anticancer therapy
PD or death after ≥ 2 consecutively missed or not evaluable (NE) disease assessments	Censored at date of last evaluable assessment prior to missed or NE assessments
No disease assessment at baseline or post-baseline assessment* for PFS	Censored at the first dosing date for PFS

*Baseline tumor assessment should be performed no more than 28 days before the start of study drug, unless otherwise specified in the protocol.

The scheduled visit assessment scheme is every 9 weeks in a 21-day dosing cycle during the study starting from C1D1 with the on-treatment imaging window of ± 7 days. The definition of 2 missed visits are 2 * (9 weeks + 7 days).

A by-patient listing of DOR will be provided by patient ID number in ascending order.



CCI

6.4. Changes From Protocol-Specified Efficacy Analyses

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

7. SAFETY ANALYSES

In general, safety analysis will be performed in the Safety Analysis Set for each cohort (Safety run-in cohort 1, Phase 2 cohort 1a, 1b and 1c respectively) and listings will be provided on the All Enrolled analysis set unless specified otherwise. Analysis of DLT was performed using the DLT evaluable analysis set for Safety Run-in evaluations which is not under the scope of this SAP.

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 Medical Dictionary for Regulatory Activities (MedDRA).

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 5.0.

7.1.3. Relationship of Adverse Events to Study Treatment

Related AEs are those for which the investigator selected “Related” on the AE CRF to the question of “Related to Study Treatment.” Summary of relationship will also be applied based on “Related to Study Treatment Magrolimab” and “Related to Study Treatment Docetaxel” separately.

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-patient data listings will show the relationship as missing.

7.1.4. Serious Adverse Events

Serious adverse events (SAEs) will be identified and captured 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 any events not present prior to the study treatment, or any events already present but worsening in either intensity or frequency following exposure to the study treatment.

The TEAE reporting period is defined as the period from the date of the first dose of study treatment up to 30 days after the date of the last dose of study treatment or the day before initiation of subsequent antineoplastic therapy, whichever comes first.

If the AE onset date is on or before the last dose date, the AE is considered as TEAE, regardless of the initiation of subsequent anti-cancer therapy.

7.1.5.2. Missing or incomplete Dates

If there was a missing or incomplete date for the start date or stop date of an AE, the most conservative approach was used for analysis.

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 date is the same as or after the month and year (or year alone if month is not recorded) of the first dosing date of any study drug, and
- The AE onset date is the same as or before the month and year (or year alone if month is not recorded) of the date corresponding to the cutoff date of TEAE period, which is defined as the 30 days after the any study drug last dosing date or the day before the initiation of new anticancer therapy (whichever is earlier)

An AE with completely missing onset and stop dates, or with the onset date missing and the 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 month and year (or year alone if month is not recorded) or later 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

A brief, high-level summary of the number of percentage of patients who experienced at least 1 TEAE in the endpoints described below will be provided by cohort in Safety Analysis Set. The number and percentage of patients who experienced at least 1 TEAE will also be summarized by SOC and PT or by PT only, by cohort.

- TEAEs
- TEAEs with Grade 3 or higher
- Treatment-related TEAEs for study drug (with indication of which study drug)
- Treatment-related AEs with grade 3 or higher for study drug (with indication of which study drug)
- TE SAEs
- TE Treatment-related SAEs for study drug (with indication of which study drug)
- TEAEs leading to discontinuation for study drug (with indication of which study drug)
- TEAEs leading to dose reduction for Docetaxel
- TEAEs leading to dose interruption or dose delay (including not administered) for study drug (with indication of which study drug)
- TEAEs leading to death

Multiple events will be counted only once per subject in each summary. Adverse events of all TEAEs, TEAEs of Grade 3 or higher, TE SAEs and TEAEs leading to death will be summarized by SOC and PT and listed first in alphabetic order of SOC and then by PT within each SOC in the descending order of overall frequency (or otherwise specified). 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 other AEs listed above will be summarized by PT only in descending order of overall frequencies (or otherwise specified).

By-patient listings for the following endpoints will also be provided in All Enrolled Analyses Set:

- All AEs indicating whether the event is treatment emergent
- All SAEs

- All Deaths
- All SAEs leading to death
- All AEs with severity of Grade 3 or higher
- All AEs leading to discontinuation of study drug (with indication of which study drug)
- All AEs leading to dose reduction of Docetaxel
- All AEs leading to dose interruption or dose delay (including not administered) of study drug (with indication of which study drug)

A summary (number and percentage of patients) of deaths for the endpoints listed below will be provided by cohort. Summary will include the following categories:

- All deaths
- Deaths within 30 days of the last dosing of study treatment
- Deaths beyond 30 days of the last dosing of study treatment

7.1.7. Additional Analysis of Adverse Events

7.1.7.1. Dose Limiting Toxicity (DLT)

In Safety run-in Cohort, a summary of DLT by PT among the DLT evaluable patients will be provided. DLT-type AEs will also be summarized in the same way, where DLT-type AEs are toxicities that met protocol specified criteria of DLTs and occurred beyond the protocol-specified DLT assessment period (onset date beyond the 21 days period).

By-patient listing of the DLT AEs and DLT-type AEs will also be provided.

7.1.7.2. Treatment-Emergent Adverse Events of Clinical Importance

The TEAE of clinical importance are defined in Table 7-1. Number and percentage of subjects with the following TEAE of clinical importance will be summarized by PT by cohort in Safety Analysis Set:

Table 7-1. Treatment Emergent Adverse Events of Clinical Importance

TEAE of Clinical Importance	Search Strategy
Anaemia	Medical Search Term (MST) Anemia Extravascular transient hemolysis
Infusion related reactions	Standardized MedDRA Queries (SMQ) Hypersensitivity (narrow) + within one day of latest infusion of any study drug
Severe Neutropenia	PT: Grade 3+ Febrile neutropenia, Grade 3+ Neutrophils count decreased, Grade 3+ Neutropenia
Serious Infections	SAE within SOC: Infections and infestations
Transfusion reactions due to magrolimab interference with RBC typing	MST Transfusion reactions due to magrolimab interference with RBC typing
Thromboembolic events	SMQ Embolic and thrombotic events (broad)
Pneumonitis	SMQ Interstitial lung disease (broad)

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 30 days plus the last dose date OR the initiation of subsequent anti-cancer therapy. If the lab data collected on or before the last dose date, data will be included regardless of the initiation of subsequent anti-cancer 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-patient listing for laboratory test results will be provided by subject ID number 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 cohort for selected laboratory test specified in the study protocol 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

Plots of lab parameters may include (but not limited to) hemoglobin, hematocrit, platelet, and absolute neutrophil counts over time.

In the case of multiple values in an analysis window, 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 (i.e., 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 and prior to the day of initiation of subsequent anti-cancer therapy. If the relevant postbaseline lab is assessed on or before the last dose date, the laboratory abnormality is considered as treatment-emergent laboratory abnormality, regardless of the initiation of subsequent anti-cancer therapy. 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. Treatment-Emergent Marked Laboratory Abnormalities

Treatment-emergent marked laboratory abnormalities are defined as values that increase from baseline by at least 3 toxicity grades at any postbaseline time point up to and including the date of last dose of study drug plus 30 days and prior to the day of initiation of subsequent anti-cancer therapy. If the relevant postbaseline lab (with at least 3 toxicity grades increasing from baseline) is assessed on or before the last dose date, the laboratory abnormality is considered as treatment-emergent marked laboratory abnormality, regardless of the initiation of subsequent anti-cancer therapy. If the relevant baseline laboratory value is missing, any Grade 3 or 4 values observed within the timeframe specified above will be considered treatment-emergent marked abnormalities.

7.2.2.3. Summaries of Laboratory Abnormalities

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

- TE Laboratory abnormalities (Grade 1 to 4 separately)
- Grade 3 or 4 TE laboratory abnormalities
- Marked TE laboratory abnormalities

For all summaries of laboratory abnormalities, the denominator is the number of patients in the correponding nonmissing postbaseline laboratory values up to 30 days after the last dosing date or the day before initiation of new anticancer therapy, whichever is earlier.

By-patients listings of treatment-emergent Grade 3 or 4 laboratory abnormalities and treatment emergent marked 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.

By-patient listing for post-infusion hematology will also be provided. Laboratory abnormalities that occur before the first dose of study drug or after the patient has been discontinued from treatment for at least 30 days will also be included in a data listing.

7.2.3. Liver-related Laboratory Evaluations

Liver-related abnormalities after the first dose of any study drug will be examined and summarized by cohort 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 30 days after the last dose of study drug or the day before initiation of new anticancer therapy, whichever is earlier. 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 and ALP, 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 at least one postbaseline visit, at which all the relevant tests are nonmissing 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

Descriptive statistics will be provided by cohort for body weight, height, BMI, systolic and diastolic blood pressure, heart rate, temperature and respiratory rate.

- Baseline values
- Values at each postbaseline time point
- Change and percentage change from baseline at each postbaseline time point

A baseline value will be defined as the last available value collected on or prior to the first dose of any study drug. Change from baseline to a postbaseline visit will be defined as the postbaseline value minus the baseline value. Vital signs measured at unscheduled visits will be included for the baseline value selection.

A by-patient listing of vital signs will be provided by subject ID number and time point in chronological order.

7.4. Electrocardiogram (ECG) Results

A by-patient listing of ECG results will be provided by subject ID number in ascending order.

7.5. Eastern Cooperative Oncology Group (ECOG) Performance Status

A by-patient listing of ECOG performance status will be provided by subject ID number in ascending order.

7.6. Pregnancy Test

A by-patient listing of the pregnancy test results as collected in CRF will be provided.

7.7. Changes From Protocol-Specified Safety Analyses

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

8. CHANGES FROM PROTOCOL-SPECIFIED ANALYSES

There is no deviation from protocol defined analysis.

9. PHARMACOKINETIC (PK) AND IMMUNOGENICITY ANALYSES

9.1. PK Analysis

The PK Analysis Set will be used for summaries of PK concentration of magrolimab versus time. Serum concentrations will be listed and summarized for magrolimab using descriptive statistics by sampling timepoint and treatment. Graphical plots of individual serum concentration versus time and mean concentration versus time by treatment will be generated. PK data from this study might be combined with PK data from other Magrolimab studies and analyzed using a population PK model. Such an analysis would be reported separately.

9.2. Immunogenicity analysis

Serum samples for antidrug antibody (ADA) assessments will be conducted utilizing a tiered approach (screen, confirmatory and titer), and ADA data will be collected at scheduled visits shown in the protocol. ADA result from each sample will be reported as either positive or negative. If the sample is positive, the ADA titer will be reported as well. In addition, the presence of neutralizing antibody (nAb) will be tested for all ADA positive samples using a ligand-binding assay. The nAb results will be reported as positive or negative.

Patients for ADA prevalence are defined as patients who had at least one positive ADA sample at any time, including baseline and post-baseline, in Immunogenicity Analysis Set.

Patients for ADA incidence are defined as patients with at least one baseline ADA sample and at least one post-treatment ADA sample in Immunogenicity Analysis Set.

Patients for nAb prevalence are defined as patients who had at least one positive nAB sample at any time, including baseline and post-baseline, in Immunogenicity Analysis Set

Among patients for ADA incidence, patients who had Treatment-Induced ADA or Treatment-Boosted ADA are categorized as ADA positive by incidence, where

- Treatment-Induced ADA is defined as patients who had negative baseline ADA sample and at least one positive post-treatment ADA sample.
- Treatment-Boosted ADA is defined as 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.

The remaining patients among patient for ADA incidence are ADA negative by incidence.

Transient ADA is defined as:

- Treatment-Induced ADA detected only at one sampling time point during the treatment or follow-up observation period (excluding the last sampling time point, which ought to be considered persistent unless shown to be undetectable at a later time)

  or

- 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 less than 16 weeks, and the patient's last sampling time point is ADA-negative.

ADA Transience Rate: the proportion of patients who had transient among patients for ADA incidence.

Persistent ADA is defined as

- 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

- Treatment-Induced ADA incidence (i.e. Treatment-induced ADA) only in the last sampling time point of the treatment study period or at a sampling time point with less than 16 weeks before an ADA-negative last sample.

- ADA Persistence Rate: the proportion of patients who had persistent ADA among patients for ADA incidence.

The following ADA categories will be summarized by cohorts.

- ADA prevalence
- ADA positive post-baseline and positive at baseline
- ADA not detected post-baseline and positive at baseline
- ADA incidence
- Treatment-induced ADA
- Treatment-boosted ADA

- Persistent ADA
- Transient ADA
- nAb prevalence

ADA titer and nAb data will be listed for samples confirmed positive for the presence of ADA to study drug. The effect of ADA on PK, safety and efficacy may be examined by descriptive summaries if data allow.

10. BIOMARKER ANALYSIS

The baseline level, absolute level, and change from baseline level over time will be summarized using descriptive statistics for each biomarker at sample collection timepoint by cohort, as appropriate. CCI [redacted]

11. REFERENCES

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Smit EF, Fokkema E, Biesma B, Groen HJ, Snoek W, Postmus PE. A phase II study of paclitaxel in heavily pretreated patients with small-cell lung cancer. Br J Cancer 1998;77 (2):347-51.

12. SOFTWARE

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

13. APPENDICES

13.1. Appendix 1. RECIST 1.1-based Assessments - Overall visit response

The RECIST tumour response data will be used to determine each patient's visit response according to RECIST version 1.1. At each visit, patients will be assigned a RECIST 1.1 visit response of CR, PR, SD or PD, using the information from target lesions (TLs), non-target lesions (NTLs) and new lesions and depending on the status of their disease compared with baseline and previous assessments. If a patient has had a tumour assessment which cannot be evaluated, then the patient will be assigned a visit response of not evaluable (NE). For patients with no disease at baseline (i.e. no TLs and no NTLs), evaluation of overall visit responses will be based on absence/presence of new lesions. If no TLs and no NTLs are recorded at a visit, both the TL and NTL visit response will be recorded as NA and the overall visit response will be no evidence of disease (NED). If a new lesion is observed then the overall visit response will be PD. Table 13-1 summarizes overall visit response given the visit responses from TL and NTL arecombined with new leision.

Table 13-1. Overall Visit Response

Target lesions	Non-target lesions	New lesions	Overall response
CR	CR or NA	No	CR
CR	Non CR/Non PD or NE	No	PR
PR	Non PD or NE or NA	No	PR
SD	Non PD or NE or NA	No	SD
NE	Non PD or NE or NA	No	NE
PD	Any	Any	PD
Any	PD	Any	PD
Any	Any	Yes	PD
NA	CR	No	CR
NA	Non CR/Non PD	No	SD
NA	NE	No	NE
NA	NA	No	NED

CR Complete response, NA Not applicable, PR Partial response, SD Stable disease, PD Progression of disease, NE Not evaluable, NED No evidence of disease.