STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 2 Study of Magrolimab Combination Therapy in Patients With Unresectable, Locally Advanced or Metastatic Triple-Negative Breast Cancer
Name of Test Drug:	Magrolimab (Hu5F9-G4)
Study Number:	GS-US-586-6144
Protocol Version (Date):	Amendment 6 (30 January 2024)
Analysis Plan Version:	2.0
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Analysis Plan Author(s):	PPD
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CONFIDENTIAL AND PROPRIETARY INFORMATION

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LIST OF ABBREVIATIONS

ADA	antidrug antibodies
AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BICR	blinded independent central review
BLQ	below the limit of quantitation
BMI	body mass index
BOR	best overall response
CI	confidence interval
CRF	case report form
CSR	clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
DLT	dose-limiting toxicity
DOR	duration of response
ECG	electrocardiogram
GDRC	Gilead Data Review Committee
KM	Kaplan Meier
IRT	interactive response technology
ITT	intent to treat
LOQ	limit of quantitation
MedDRA	Medical Dictionary for Regulatory Activities
mITT	modified intent-to-treat
mTNBC	metastatic triple-negative breast cancer
NCI	National Cancer Institute
ORR	objective response rate
OS	overall survival
PFS	progression-free survival
PK	pharmacokinetics
PRO	patient reported outcome
PT	preferred term
Q1, Q3	first quartile, third quartile
RECIST	Response Evaluation Criteria in Solid Tumors
RP2D	Recommended Phase 2 dose
SAP	statistical analysis plan
StD	standard deviation
SI (units)	international system of units
SOC	system organ class
SRT	Safety Review Team

TEAE	treatment-emergent adverse event
TFLs	tables, figures, and listings
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 the informal interim, primary and final analyses of Study GS-US-586-6144. This SAP is based on the study protocol amendment 6 dated 30 Janurary 2024. Any changes made after the finalization of the SAP will be documented in the clinical study report (CSR).

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 Objective(s)	Primary Endpoint(s)
Safety Run-in Cohort 1: • To evaluate the safety, tolerability, and recommended Phase 2 dose (RP2D) of magrolimab in combination with nab-paclitaxel or paclitaxel Phase 2 Cohort 1: • To compare the efficacy of magrolimab in combination with nab-paclitaxel or paclitaxel versus nab-paclitaxel or paclitaxel alone as determined by progression-free survival (PFS) by investigator assessment Safety Run-in Cohort 2: • To evaluate the safety, tolerability, and RP2D of magrolimab in combination with sacituzumab govitecan Cohort 2 (Safety Run-in Cohort 2 and Phase 2 Cohort 2): • To evaluate the efficacy of magrolimab in combination with sacituzumab govitecan as determined by confirmed objective response rate (ORR) by investigator assessment	Safety Run-in Cohorts 1 and 2: • Incidence of dose-limiting toxicities (DLTs), adverse events (AEs), and laboratory abnormalities according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE), Version 5.0 Phase 2 Cohort 1: • PFS, defined as the time from the date of randomization until the earliest date of documented disease progression as determined by investigator assessment using Response Evaluation Criteria in Solid Tumors (RECIST), Version 1.1, or death from any cause, whichever occurs first Cohort 2 (Safety Run-in Cohort 2 and Phase 2 Cohort 2): • Confirmed ORR (defined as the proportion of patients who achieve complete response or partial response that is confirmed at least 4 weeks after initial documentation of response), as determined by invesrigator assessment per RECIST, Version 1.1

Secondary Objective(s)	Secondary Endpoint(s)
Phase 2 Cohort 1: • To compare the efficacy between treatment arms by ORR by investigator assessment • To compare the efficacy between treatment arms by additional measures of efficacy, including duration of response (DOR) and overall survival (OS) • To compare the safety and tolerability between treatment arms Cohort 2 (Safety Run-in Cohort 2 and Phase 2 Cohort 2): • To evaluate PFS by investigator assessment • To evaluate additional measures of efficacy of magrolimab in combination with sacituzumab govitecan, including DOR and OS • Safety and tolerability of magrolimab in combination with sacituzumab govitecan Safety Run-in Cohorts 1 and 2 and Phase 2 Cohorts 1 and 2: To evaluate the pharmacokinetics (PK) and immunogenicity of magrolimab in combination with anticancer chemotherapies	Phase 2 Cohort 1 and Cohort 2 (Safety Run-in Cohort 2 and Phase 2 Cohort 2): • Confirmed ORR, as determined by investigator assessment per RECIST, Version 1.1 (only for Phase 2 Cohort 1) • PFS, as determined by investigator assessment per RECIST, Version 1.1, or death from any cause, whichever occurs first (only for Cohort 2) • DOR, defined as time from first documentation of complete response or partial response to the earliest date of documented disease progression as determined by investigator assessment, per RECIST, Version 1.1, or death from any cause, whichever occurs first • OS, defined as time from date of randomization to death from any cause • Incidence of AEs and laboratory abnormalities according to NCI CTCAE, Version 5.0 Safety Run-in Cohorts 1 and 2 and Phase 2 Cohorts 1 and 2: • Magrolimab concentration versus time and antidrug antibodies (ADA) to magrolimab

1.2. Study Design

This is a Phase 2, randomized (Phase 2 Cohort 1 only), open-label, multicenter study to evaluate magrolimab in combination with either nab-paclitaxel or paclitaxel for patients with untreated, unresectable, locally advanced or metastatic triple-negative breast cancer (mTNBC) and magrolimab in combination with sacituzumab govitecan for patients with unresectable, locally advanced or mTNBC who have received at least 1 and no more than 2 prior lines of treatment in the advanced setting. This study will consist of 2 Safety Run-in Cohorts:

- **Safety Run-in Cohort 1:** magrolimab in combination with the choice of nab-paclitaxel or paclitaxel administered in patients previously untreated for unresectable, locally advanced or mTNBC whose tumors are not appropriate for immune checkpoint inhibitor therapy.

- **Safety Run-in Cohort 2:** magrolimab in combination with sacituzumab govitecan in patients with unresectable, locally advanced or mTNBC who have received at least 1 and no more than 2 prior lines of treatment in the unresectable, locally advanced or metastatic setting.

Initially, up to 6 patients will be enrolled in each safety run-in cohort at a starting dose level. A DLT evaluation period of 1 cycle (28 days) for Cohort 1 and (21 days) for Cohort 2 will occur.

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.

Approximately 18 patients (each cohort) could be potentially enrolled and evaluated during the safety run-in cohorts.

If a patient experiences a DLT during the DLT assessment period, the patient will discontinue treatment. Patients who are not evaluable for DLT assessment in the Safety Run-in Cohorts will be replaced. The DLT definition is provided in the protocol.

Once Safety Run-in Cohort 1 is completed and RP2D for magrolimab in combination with either nab-paclitaxel or paclitaxel is determined, the sponsor will open Phase 2 Cohort 1.

- **Phase 2 Cohort 1:** In this open-label, randomized, 2-arm cohort, unresectable, locally advanced or mTNBC patients will be randomized in a 1:1 ratio to receive either magrolimab in combination with the choice of nab-paclitaxel or paclitaxel (Experimental Arm A) or nab-paclitaxel or paclitaxel (Control Arm B). The primary efficacy assessment will be investigator-assessed PFS. In the original study design the primary analysis was to occur after 63 events; however, due to the early closure of Phase 2 Cohort 1, the primary analysis will occur when every enrolled patient has approximately a minimum of 6 months follow-up. Stratification factors for randomization include the following: 1) receipt versus nonreceipt of neoadjuvant and/or adjuvant taxane therapy, 2) presence versus absence of liver metastases, 3) treatment with nab-paclitaxel versus paclitaxel.

Once Safety Run-in Cohort 2 is completed and the RP2D for magrolimab in combination with sacituzumab govitecan is determined, the sponsor will open Phase 2 Cohort 2.

- **Phase 2 Cohort 2:** In this open-label single-arm cohort, unresectable, locally advanced or mTNBC patients who have received at least 1 and no more than 2 prior lines of treatment in the unresectable, locally advanced or metastatic setting will receive magrolimab in combination with sacituzumab govitecan. The primary efficacy assessment will be investigator-assessed confirmed ORR.

Phase 2 cohorts treatment-related toxicity for the magrolimab combination therapies (magrolimab + nab-paclitaxel or paclitaxel in Phase 2 Cohort 1 and magrolimab + sacituzumab govitecan in Phase 2 Cohort 2) will be monitored by Gilead Data Review Committee (GDRC) at a preset frequency.

Study treatments for Safety Run-in Cohort 1 and for Phase 2 Cohort 1 are shown in Table 1-1 and Table 1-2, respectively. Nab-paclitaxel or paclitaxel use will be per investigator discretion and in accordance with local guidelines and practices.

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

Drug	Dose Level	Dose Schedule (Cycles are 28 Days)		
		Cycle 1	Cycle 2	Cycle 3+
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, 15, and 22	30 mg/kg IV (2 h ± 30 min) on Days 1, 8, 15, and 22	30 mg/kg IV (2 h ± 30 min) on Days 1 and 15
	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, 15, and 22	20 mg/kg IV (2 h ± 30 min) on Days 1, 8, 15, and 22	20 mg/kg IV (2 h ± 30 min) on Days 1 and 15
	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, 15, and 22	15 mg/kg IV (2 h ± 30 min) on Days 1, 8, 15, and 22	15 mg/kg IV (2 h ± 30 min) on Days 1 and 15
Nab-paclitaxel	100 mg/m^2	100 mg/m^2 IV on Days 1, 8, and 15	100 mg/m^2 IV on Days 1, 8, and 15	100 mg/m^2 IV on Days 1, 8, and 15
Paclitaxel	90 mg/m^2	90 mg/m^2 IV on Days 1, 8, and 15	90 mg/m^2 IV on Days 1, 8, and 15	90 mg/m^2 IV on Days 1, 8, and 15

IV = intravenous

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

Drug	Dose Schedule (Cycles are 28 Days)		
	Cycle 1	Cycle 2	Cycle 3+
Magrolimab (Arm A only) 1 mg/kg IV (3 h ± 30 min)	Day 1 (priming dose)		
Magrolimab (Arm A only) RP2D[a] IV (2 h ± 30 min)	Days 8, 15, and 22	Days 1, 8, 15, and 22	Days 1 and 15
Nab-paclitaxel (Arms A and B) 100 mg/m^2 IV	Days 1, 8, and 15	Days 1, 8, and 15	Days 1, 8, and 15
Paclitaxel (Arms A and B) 90 mg/m^2 IV	Days 1, 8, and 15	Days 1, 8, and 15	Days 1, 8, and 15

IV = intravenous; RP2D = recommended Phase 2 dose

a RP2D as determined in the Safety Run-in Cohort.

Study treatments for Safety Run-in Cohort 2 and for Phase 2 Cohort 2 are shown in Table 1-3 and Table 1-4, respectively. Sacituzumab govitecan use will be in accordance with local standard practices or current local prescribing information:

Table 1-3. Safety Run-in Cohort 2: Dose Level, Schedule, and De-escalation

Drug	Dose Level	Dose Schedule (Cycles are 21 Days)		
		Cycle 1	Cycle 2	Cycle 3+
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
Sacituzumab govitecan	10 mg/kg	10 mg/kg IV (3 h ± 30 min) on Days 1 and 8	10 mg/kg IV (1 to 2 h ± 30 min) on Days 1 and 8	10 mg/kg IV (1 to 2 h ± 30 min) on Days 1 and 8

IV = intravenous

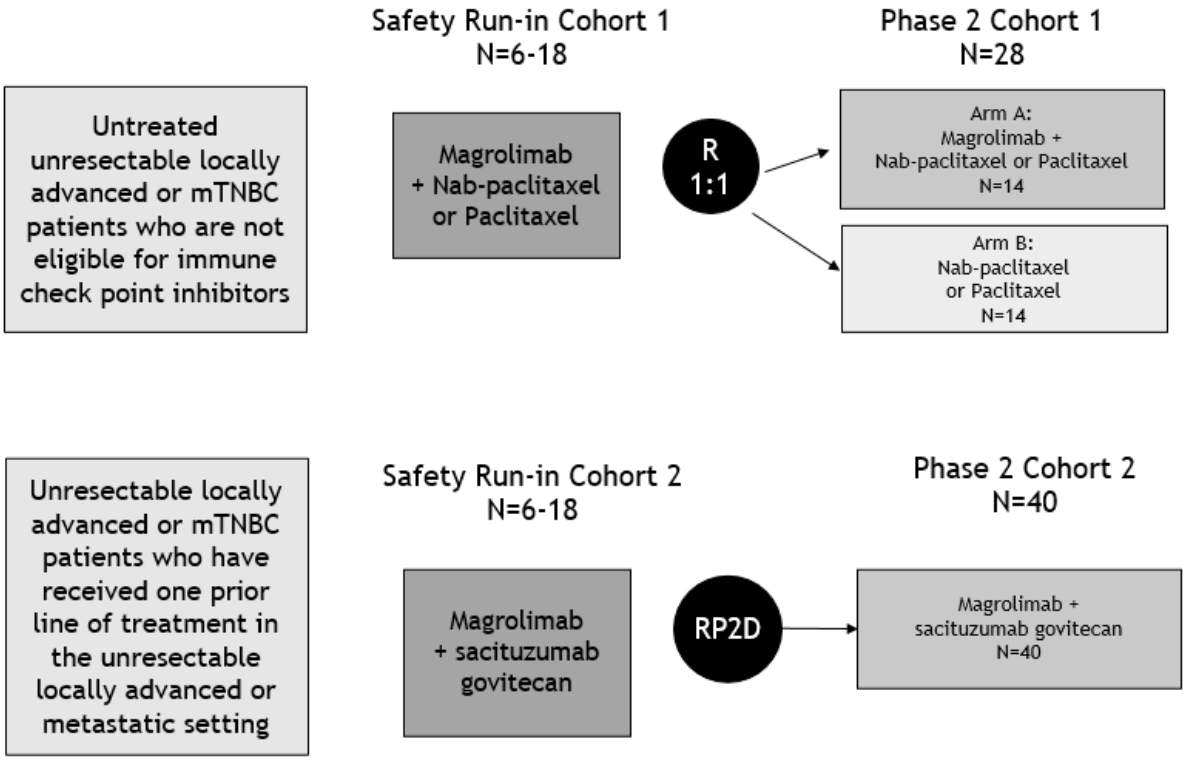
Table 1-4. Phase 2 Cohort 2: Dose Level and Schedule

Drug	Dose Schedule (Cycles are 21 Days)		
	Cycle 1	Cycle 2	Cycle 3+
Magrolimab 1 mg/kg IV (3 h ± 30 min)	Day 1 (priming dose)		
Magrolimab RP2D[a] IV (2 h ± 30 min)	Days 8, and 15	Days 1, 8, and 15	Days 1
Sacituzumab govitecan 10 mg/kg IV	Days 1 and 8 (3 h ± 30 min)	Days 1 and 8 (1 to 2 h ± 30 min)	Days 1 and 8 (1 to 2 h ± 30 min)

IV = intravenous; mTNBC = metastatic triple-negative breast cancer; RP2D = recommended Phase 2 dose
a RP2D as determined in the Safety Run-in Cohort.

Patient participation will include screening, randomization (Phase 2 Cohort 1 only), treatment, and follow-up. Screening will last up to 30 days before the first dose of study treatment, during which time the patient's eligibility and baseline characteristics will be determined. Patients will receive study treatment according to the dose schedule in protocol Appendix Table 1 and Appendix Table 2. Cycle lengths are 28 days for Safety Run-in Cohort 1 and Phase 2 Cohort 1. Cycle lengths are 21 days for Safety Run-in Cohort 2 and Phase 2 Cohort 2. Patients may continue treatment unless they develop unacceptable toxicity that cannot be clinically managed by dose or schedule modifications. Patients who discontinue all study drugs will be followed for safety, disease progression, and survival. All patients will be followed for survival until death, withdraw from consent, lost to follow-up, and the end of study, whichever occurs first.

The study schematic is provided below.



Based on the original design, approximately 168 patients may be enrolled in the study, including 92 randomized patients in Phase 2 Cohort 1. Due to the early closure of Phase 2 Cohort 1, approximately 104 patients may be enrolled in the study, including 6-18 patients in Safety Run-in Cohort 1, 28 randomized patients in Phase 2 Cohort 1, 6-18 patients in Safety Run-in Cohort 2 and 40 patients in Phase 2 Cohort 2.

1.3. Sample Size and Power

Safety Run-in Cohort 1 and 2 planned for 6-18 patients in each cohort. In each cohort, initially, up to 6 patients will be enrolled at the starting dose level. 12 more patients can be potentially enrolled if dose de-escalation decision is made by a safety review team (SRT) review of according to the DLT evaluation of 1 cycle (28 days for Safety Run-in Cohort 1, 21 days for Safety Run-in Cohort 2).

Based on the original design, for Phase 2 Cohort 1, using an unstratified log-rank test, a total of 63 PFS events provides 82% power at a 1-sided alpha of 0.15 to detect a hazard ratio of 0.61 (assuming median PFS of at least 9 months compared to a control arm median PFS of 5.5 months). Assuming an accrual period of 15 months, a minimum follow-up time of 6 months, and a 5% annual drop-out rate, 92 patients (46 patients per arm) would be required to obtain 63 events.

Due to the early closure of Phase 2 Cohort 1, approximately 28 patients have been enrolled and randomized for Arm A and Arm B. The analysis of the PFS given the current sample size is under powered and will be descriptive only.

For Cohort 2 (Safety Run-in Cohort 2 and Phase 2 Cohort 2), patients treated at the selected Phase 2 Cohort 2 dose level, using chi-square test, a total of 46 patients (including 6 patients in Safety Run-in Cohort 2 and 40 patients in Phase 2 Cohort 2) provides 88% power at a 1-sided alpha of 0.15 to detect an ORR of 50% compared with a null ORR of 34%.

Power calculations were performed using EAST 6.5.

2. TYPE OF PLANNED ANALYSIS

2.1. Interim Analyses

2.1.1. Dose Determination Analysis

For the purposes of making the dose de-escalation decisions for the Safety Run-in Cohorts, dose-determination analyses of relevant safety data focusing on DLTs and overall safety profile will be conducted by the sponsor after all patients in the DLT-Evaluable Analysis Set have completed the required DLT assessment period.

Dose de-escalation decisions will be made for the Safety Run-in Cohort 1 and Safety Run-in Cohort 2 as follows:

- If 2 or less of 6 DLT-evaluable patients experience a DLT in Cycle 1, enrollment into Phase 2 Cohort 1 or Phase 2 Cohort 2 will begin at this dose level as the RP2D.
- If more than 2 patients experience at least one 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.

Dose de-escalation for the Safety Run-in Cohorts is presented in Table 1-1 and Table 1-3. Based on the totality of the data, alternative doses of magrolimab not described in Table 1-1 or Table 1-3 may be considered for dose de-escalation by the Safety Review Team (SRT) and sponsor.

The recommended dose for Phase 2 Cohort 1 and Phase 2 Cohort 2 will be determined based on all relevant clinical and PK data from all patients treated in the safety run-in phase, including the data on safety during a longer follow up after the DLT assessment period. A SRT will be established to assess safety of the patients. Detailed construction can refer to the SRT charter.

2.1.2. Treatment-related Toxicity Monitoring Analysis for Phase 2 Cohorts

For Phase 2 Cohort 1 Arm A, Treatment-related toxicity will be monitored by a Gilead Data Review Committee (GDRC) at a preset frequency with stopping boundaries listed in Table 2-1 after the safety data of the first 12 treated patients in Phase 2 Cohort 1 Arm A from at least 1 cycle of follow-up become available. From the original design where 46 patients were planned to be enrolled for Phase 2 Cohort 1 Arm A, a second GDRC review was planned when safety data of 36 patients from the first 3 cycles of follow-up become available. Given the early closure of Phase 2 Cohort 1, a total of 14 patients have been enrolled for Phase 2 Cohort 1 Arm A; therefore, only the first GDRC at N = 12 will occur. The ongoing treatment will stop when the number of patients with either Grade 4 or 5 treatment-related treatment-emergent adverse events (TEAEs) or treatment-related deaths meet the criteria. Bayesian toxicity monitoring {Lee 2021} based on beta-binomial model was used to derive the boundaries. Noninformative prior distribution of Beta (0.5, 0.5) for the true toxicity rate (θ) of Grade 4 or 5 treatment-related TEAEs is used, and excessive toxicity can be claimed when $P(\theta \geq 0.18|n, r) \geq 0.9$.

The '*n*' and '*r*' are the sample size and number of patients with specific events at the interim analysis for toxicity monitoring, respectively. Maximum toxicity rate was assumed at 18%, where the excessive toxicity can be claimed if the posterior probability of excessive toxicity is higher than or equal to threshold at 90%. The probabilities of early stopping are 2.6%, 15.5%, and 50.8% when the true rates are 10%, 18%, and 30%, respectively. Similarly, noninformative prior distribution of Beta (0.25, 0.25) for the true toxicity rate of treatment-related death is used with maximum toxicity rate and threshold assumed as 2.5% and 90%, respectively. The probabilities of early stopping are 0.6%, 3.5%, and 11.8% when the true rates are 1%, 2.5%, and 5%, respectively.

For Phase 2 Cohort 2, treatment-related toxicity will be monitored by GDRC at a preset frequency with stopping boundaries listed in Table 2-2 after the first 10 patients are treated at the dose level for Phase 2 Cohort 2 for at least 1 cycle of follow-up, and thereafter when safety data from 30 patients from the first 3 cycles of follow-up become available. Same prior distribution as above are assumed. For Grade 4 or 5 treatment-related TEAEs, maximum toxicity rate and threshold are assumed as 40% and 90%, respectively. The probabilities of early stopping are 2.0%, 21.1%, and 73.1% when the true rates are 25%, 40%, and 55%, respectively. For treatment-related deaths, maximum toxicity rate and threshold are assumed as 2.5% and 90%, respectively. The probabilities of early stopping are 0.7%, 5.2%, and 21.5% when the true rates are 1%, 2.5%, and 5% respectively.

Table 2-1. Stopping Boundary Due to Toxicity (Phase 2 Cohort 1 Arm A)

	N=12
Grade 4/5 treatment-related TEAEs	≥ 4
Treatment-related deaths	≥ 2

TEAE = treatment-emergent adverse event

Table 2-2. Stopping Boundary Due to Toxicity (Phase 2 Cohort 2)

	N=10	**N=30**
Grade 4/5 treatment-related TEAEs	≥ 6	≥ 16
Treatment-related deaths	≥ 2	≥ 3

TEAE = treatment-emergent adverse event

2.2. Informal Interim Analysis

For the informal interim analysis, interim efficacy and safety analyses are planned at approximately 13 weeks after 20 subjects are treated with magrolimab at the recommended Phase 2 dose in the Safety Run-in Cohort 2 and Phase 2 Cohort 2.

2.3. Primary Analysis

For the primary analysis, outstanding data queries will have been resolved or adjudicated as unresolvable, and the data will have been cleaned and finalized for the analysis.

For Phase 2 Cohort 1, the primary analysis of PFS will be conducted after every enrolled patient has approximately a minimum of 6 months follow-up.

For Cohort 2 (Safety Run-in Cohort 2 and Phase 2 Cohort 2), the primary analysis of ORR will be conducted when all enrolled patients have approximately a minimum of 6 months follow-up.

Due to the determination of the program, primary analysis is canceled.

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 treatment group.

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. Intent-to-Treat (ITT) Analysis Set

Intent-to-treat (ITT) Analysis Set includes all patients who were randomized in the Phase 2 Cohort 1. This is the primary analysis set for efficacy analyses for Phase 2 Cohort 1.

3.1.3. Modified ITT (mITT) Analysis Set

The mITT Analysis Set includes all enrolled patients who took at least 1 dose of study drug. This is the primary analysis set for efficacy analyses for Phase 2 Cohort 2.

3.1.4. Safety Analysis Set

The Safety Analysis Set includes all patients who took at least 1 dose of any study drug. Analysis will be conducted according to the actual treatment received. This is the primary analysis set for safety analyses, except for DLTs.

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

For Safety Run-in Cohort 1, the primary analysis set for the DLT analysis is the DLT-Evaluable Analysis Set, defined as all patients who meet 1 of the following criteria in the DLT assessment period:

- 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 3 infusions of magrolimab (28-day cycle), and at least 2 doses of nab-paclitaxel or paclitaxel in Safety Run-in Cohort 1.

For Safety Run-in Cohort 2, the primary analysis set for the DLT analysis is the DLT-Evaluable Analysis Set, defined as all patients who meet 1 of the following criteria in the DLT assessment period:

- 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 2 infusions of sacituzumab govitecan in Safety Run-in Cohort 2.

Patients who are not evaluable for DLT assessment in the Safety Run-in Cohorts will be replaced by other patients who will be enrolled at the same dose level. For patients who are replaced but received at least 1 dose of any study drug, they will be included in the Safety Analysis Set and not in the DLT-Evaluable Analysis Set.

3.1.6. Pharmacokinetic Analysis Set

The Pharmacokinetic (PK) Analysis Set, is defined as all patients who received any amount of magrolimab and have at least 1 evaluable post-treatment serum concentration of magrolimab.

3.1.7. Immunogenicity Analysis Set

The Immunogenicity Analysis Set will include all participants who received any amount of magrolimab and have at least 1 evaluable anti-magrolimab antibody test results.

3.2. Subject Grouping

3.2.1. Subject Grouping for Each Analysis Set

For analyses based on the ITT Analysis Set, patients will be grouped according to the treatment to which they were randomized. For analysis based on All Enrolled Analysis Set and mITT Analysis Set, patients will be grouped according to the planned treatment. For analyses based on the Safety Analysis Set and DLT-Evaluable Analysis Set, patients will be grouped according to the actual treatment received. The actual treatment received will differ from the randomized treatment only when their actual treatment differs from randomized treatment for the entire treatment duration.

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

3.2.2. Subject Grouping for Each Type of Analysis

3.2.2.1. Informal Interim Analysis

For patients who are in in Safety Run-In Cohort 2 and Phase 2 Cohort 2, the informal interim analysis is planned at approximately 13 weeks after 20 subjects are treated with magrolimab at the RP2D. The efficacy endpoints will be analyzed using mITT analysis set. The safety endpoints will be analyzed using Safety Analysis Set. Patients will be pooled from Safety Run-In Cohort 2 and Phase 2 Cohort 2.

3.2.2.2. Primary Analysis

For Phase 2 Cohort 1, the primary analysis of PFS will be conducted after all enrolled patients have approximately a minimum of 6 months follow-up. Efficacy for Safety Run-In Cohort 1 will be listed only. Efficacy endpoints for Phase 2 Cohort 1 will be summarized by treatment group using ITT analysis set. Safety and other analyses will be summarized for Safety Run-In Cohort 1 and Phase 2 Cohort 1 by phase and treatment group.

For Cohort 2, the primary analysis of ORR will be conducted approximately 6 months after the last patient is enrolled in the Phase 2. Efficacy, safety and other analyses will be summarized by pooled Safety Run-In Cohort 2 and Phase 2 Cohort 2.

Due to the determination of the program, primary analysis is canceled.

3.2.2.3. Final Analysis

Efficacy for Safety Run-In Cohort 1 will be listed only. Efficacy endpoints for Phase 2 Cohort 1 will be summarized by treatment group using ITT analysis set. Safety and other analyses will be summarized for Safety Run-In Cohort 1 and Phase 2 Cohort 1 by phase, treatment group, and pooled Safety Run-in Cohort 1 and Phase 2 Cohort 1 Arm A.

For Phase 2 Cohort 2, the descriptive analysis of ORR will be summarized based on the mITT analysis set. Efficacy for Safety Run-In Cohort 2 will be listed only. Safety and other analyses will be summarized by phase.

3.3. Strata and Covariates

Patients in Phase 2 Cohort 1 who meet eligibility criteria will be randomized in a 1:1 ratio to magrolimab in combination with nab-paclitaxel or paclitaxel or either nab-paclitaxel or paclitaxel using interactive response technology (IRT). Nab-paclitaxel or paclitaxel use will be per investigator discretion and in accordance with local guidelines and practices.

Randomization will be stratified by 1) receipt versus nonreceipt of neoadjuvant and/or adjuvant taxane therapy, 2) presence versus absence of liver metastases, and 3) treatment with nab-paclitaxel versus paclitaxel. If there are discrepancies in stratification factor values between the IRT and the clinical database, the values recorded in the IRT will be used for the primary analyses.

Due to the small sample size in Phase 2 Cohort 1, stratified analyses are not required for Phase 2 Cohort 1. Stratified analyses are not applicable to Safety Run-in Cohorts or Phase 2 Cohort 2 of the study. Detailed analysis methods are discussed in Section 6.

3.4. Examination of Subject Subgroups

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

3.5. Adjustment for Multiplicity

CCI [redacted]

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 Study 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. For screen failures or patients who are not enrolled or randomized, the date the first informed consent was signed will be used for the age derivation. For patients enrolled or randomized but not dosed with any study drug, the enrollment or randomization date 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 at the same precision level of the originally reported value 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"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.

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 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 participant is enrolled or randomized but not dosed, the enrollment or randomization date will be study day 1.

3.8.2. Analysis Visit Windows

Subject visits might not occur on protocol-specified days. Therefore, for the purpose of analysis, observations will be assigned to analysis windows.

The analysis windows for lab assessments are provided in Table 3-1 and Table 3-2. Post-infusion lab assessments for hemoglobin will use nonimal visit and will be excluded when applying Table 3-1 and Table 3-2.

Table 3-1. Analysis Visit Windows for Lab By-visit Summaries in Safety Run-in Cohort 1 and Phase 2 Cohort 1 (Hematology and Chemistry, excluding Haptoglobin, LDH, Urianalysis or Coagulation)

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	46
Week 7	50	47	53
Week 8	57	54	60
Week 9	64	61	67
Week 10	71	68	77
Week xx[d]	(xx)*7 + 1	(xx)*7 - 6	(xx)*7 + 4
Week (xx+1)[d]	(xx+1)*7 + 1	(xx+1)*7 – 2	(xx+1)*7 + 4
Week (xx+2)[d]	(xx+2)*7 + 1	(xx+2)*7 – 2	(xx+2)*7 + 7

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, 16, 20, 24 etc.

Table 3-2. Analysis Visit Windows for Lab By-visit Summaries in Safety Run-in Cohort 2 and Phase 2 Cohort 2 (Hematology and Chemistry, excluding Haptoglobin, LDH, Urianalysis or Coagulation)

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	46
Week 7	50	47	56
Week xx[d]	(xx)*7 + 1	(xx)*7 - 6	(xx)*7 + 4
Week (xx+1)[d]	(xx+1)*7 + 1	(xx+1)*7 – 2	(xx+1)*7 + 7

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 = 9, 12, 15, 18, 21 etc.

The analysis windows for PRO in Phase 2 Cohort 1 are provided in Table 3-3.

Table 3-3. Analysis Visit Windows for By-visit Summaries of PRO assessments in Phase 2 Cohort 1

Analysis Visit	Nominal Study Day	Visit Window Study Day	
		Lower Limit	Upper Limit
Baseline		(none)	1
Week 4	29	2	43
Week 8	57	44	71
Week 12	85	72	99
Week xx[a]	(xx)*7 + 1	(xx)*7 - 12	(xx)*7 + 15

a xx = 16, 20, 24 etc.

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

If multiple valid, nonmissing measurements exist in the same visit, 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 (and prior to first dosing time) 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 best severity for categorical data.

- For postbaseline values:

  — The record closest to the nominal study 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

- Missed and Virtual Visits due to COVID-19

- Adverse events due to COVID-19

- Death due to COVID-19

- Overall assessment of COVID-19 pandemic impact

4. PROTOCOL DEVIATIONS

Patients who did not meet at least one eligibility criterion for study entry but who were enrolled/randomized in the study will be summarized by treatment group and cohorts regardless of whether they were exempted by the sponsor or not, based on the ITT Analyses Set for Phase 2 Cohort 1 and All Enrolled Analysis Set for each Safety Run-in Cohort and Phase 2 Cohort 2. 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 treatment group and cohorts based on the ITT Analysis Set for Phase 2 Cohort 1 and All Enrolled Analysis Set for each Safety Run-in Cohort and Phase 2 Cohort 2. A by-subject listing will be provided for those patients with important protocol deviation.

5. SUBJECT INFORMATION

Generally, listing and disposition table will be based on ITT Analyses Set for Phase 2 Cohort 1 and All Enrolled Analysis Set for each Safety Run-in of Cohorts and Phase 2 Cohort 2. Summary of treatment exposure, prior medications, concomitant medications and post-treatment anti-cancer therapies will use Safety Analysis Set. The remaining table summaries in this section will be based on ITT Analyses Set for Phase 2 Cohort 1 and mITT Analysis Set for Safety Run-in Cohorts and Phase 2 Cohort 2, unless specified otherwise.

5.1. Patient Enrollment and Disposition

Key study dates, including first patient screened, first patient enrolled or randomized (Phase 2 Cohort 1 only), last patient enrolled or randomized (Phase 2 Cohort 1 only) and last patient last visit for the primary endpoint for each cohort and phase, and last patient last visit for the clinical study report will be provided.

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

A similar enrollment table will be provided by randomization stratification group for Phase 2 Cohort 1 only. If there are discrepancies in the value used for stratification assignment between the IRT and the clinical database, the value collected in IRT will be used for the summary.

A summary of patient disposition will be provided by cohort and treatment group. This summary will present the the number of patients enrolled or randomized (Phase 2 Cohort 1 only), the number of patients enrolled or randomized but not dosed and the number of patients in each of the categories listed below for each cohort:

- Safety Analysis Set
- Continuing study treatment (for each study drug)
- Discontinued study drug (for each study drug) with reasons for treatment discontinuation for the correscponding drug
- 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 specific analyses set corresponding to that column.

The following by-subject 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

The study drugs include magrolimab, nab-paclitaxel, paclitaxel and sacituzumab govitecan. Extent of exposure to study treatment will be summarized using descriptive statistics for total duration of exposure to each study drug, total number of infusions for each study drug, total number of cycles received for each study drug, total cumulative dosage (mg/kg) administered for each study drug, relative dose intensity (%) of each study drug, and number (%) of patients with dose modifications (i.e. infusion interuption, dose delayed or not administered) and reasons by cohort and treatment group.

The choice of nab-paclitaxel or paclitaxel is determined by site investigator at the time of enrollment or randomization, and it is not expected to switch between nab-paxlitaxel or paclitaxel. In case a drug switch occurred for a subject, the subject will be summarized under the initial drug that the subject was assigned, unless specified otherwise.

5.2.1. Duration of Exposure to Study Drug

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

The total duration of exposure to each study drug will be summarized using descriptive statistics for continuous variables, as well as using the number (i.e., cumulative counts) and percentage of patients exposed for at least the following time periods: 1 day, 3 weeks, 6 weeks, 9 weeks, 12 weeks, 15 weeks, 18 weeks, 21 weeks and 24 weeks etc, for Cohort 2; and 1 day, 4 weeks, 8 weeks, 12 weeks, 16 weeks, 20 weeks, and 24 weeks, etc, for Cohort 1.

5.2.2. Relative Dose Intensity

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

Relative dose intensity will be summarized by below formula for each study drug:

$$\text{Relative Dose Intensity (\%)} = \frac{Total\ Amount\ of\ Study\ Drug\ Administered}{Total\ Amount\ of\ Study\ Drug\ Expected\ to\ be\ Administered} \times 100$$

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

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

5.3. Demographics and Baseline characteristics

Demographic summaries will include age, sex, race and ethnicity. Baseline characteristics will include a summary of body weight [in kg], height [in cm], body mass index [BMI; in kg/m^2], Body Surface Area [BSA; in m^2]), ECOG performance status and randomization stratification factors. The analysis will be performed for ITT Analysis Set for Phase 2 Cohort 1, and for mITT Analysis Set for Safety Run-in Cohorts and Phase 2 Cohort 2.

By-patient listing will be generated by cohort, treatment group and patient ID number.

5.4. Breast Cancer History

Time from initial diagnosis to enrollment or randomization, breast cancer laterality, number of lymph nodes resected with number and percentage of positive lymph nodes for each subject, visceral disease and location of visceral disease, diagnosis of breast cancer confirmed by histopathology (yes/no) and histological subtypes, differentiation and nuclear grade (pleomophism), disease stage at diagnosis and at screening, primary tumor classification/lymphnode classification/metastasis classification at diagnosis and at screening, ER or PR status and examination results (<1%, between 1-10% and >10%), HER2 metastatic receptor status and by test method, PD-L1 qualitative test status will be summarized using descriptive statistics for continuous variables and using number and percentage of patients for categorical variables.

A by-patient listing including all the above information will be provided.

5.5. Prior Anti-cancer Therapy

Prior adjuvant/neoadjuvant therapy (yes/no) will be summarized for Safety Run-in Cohort 1, Phase 2 Cohort 1.

Prior metastatic therapy (yes/no), number of prior regimens in metastatic setting, reason for administration (neoadjuvant, adjuvant, metastatic and other), best response for the last therapy before entering study and time from last disease progression to enrollment date will be summarized for Cohort 2.

Prior anti-cancer therapy will be coded using the World Health Organization (WHO) Drug Dictionary and summarized by Preferred Drug Name.

A by-patient listing including information collected in prior anti-cancer threapy eCRF and all derived information above will be provided.

5.6. 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.

5.7. 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.

5.8. Medical History

Medical history will be collected at screening for disease-specific and general conditions (i.e., conditions not specific to the disease being studied). General medical history will be coded using the current version of Medical Dictionary for Regulatory Activities (MedDRA). Disease-specific medical history will be summarized by cohort and treatment group for each condition.

A by-patient listing for general medical history and the coded terms including SOC and PT will be provided.

5.9. 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.

5.9.1. 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 patients for each 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 patients who received that medication. Medications may appear under multiple ATC drug classes. The summary will be ordered alphabetically by ATC drug class and then by preferred term in order of descending overall frequency within each ATC drug 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.

5.9.2. Concomitant Medications

Concomitant medications are defined as medications taken while a patient took study treatment. Use of concomitant medications will be summarized by ATC drug class Level 2 and preferred name using the number and percentage of patients for each cohort, phase, dose level and treatment group. 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 drug class and then by preferred term in descending overall frequency within each ATC drug 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 the 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. 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.

5.10. On Study Treatment and Post Study Treatment Anti-cancer Therapies

All on study treatment and post treatment anti-cancer therapies including flag for on-study treatment and post study treatment therapies will be provided in a by-patient listing sorted by patient ID number and administration date in chronological order. Note that anti-cancer therapy (other than study drugs) are not allowed during the study drug treatment per protocol. The analysis will be performed for Safety Analysis Set.

6. EFFICACY ANALYSES

Generally, summary of efficacy endpoints in this section will be based on ITT Analyses Set for Phase 2 Cohort 1 and mITT Analysis Set for Phase 2 Cohort 2, unless specified otherwise. Listing will be based on ITT Analysis Set for Phase 2 Cohort 1 and All Enrolled Analysis Set for each Safety Run-in Cohorts and Phase 2 Cohort 2.

6.1. Primary Efficacy Endpoints

6.1.1. Definition of the Primary Efficacy Endpoints

For Phase 2 Cohort 1, the primary efficacy endpoint is PFS by investigator assessment, defined as the time from the date of randomization until the earliest date of the first documented disease progression as determined based on response evaluation criteria in solid tumors (RECIST), Version 1.1 {Eisenhauer 2009}, or death from any cause.

For Safety Run-in Cohort 2 and Phase 2 Cohort 2 participants who are dosed at the selected Phase 2 Cohort 2 dose level, the primay efficacy endpoint is the objective response rate (ORR), defined as the proportion of participants who achieve complete response or partial response that is confirmed at least 4 weeks after initial documentation of response, as determined by investigator assessment per RECIST, Version 1.1. Tumor response assessments after the date of participants receiving new anticancer therapy will be excluded from the analysis. Participants who do not have baseline or on-study response status assessment or received new anticancer therapy prior to achieving CR or PR, will be considered as non-responders.

6.1.2. Analysis of the Primary Efficacy Endpoint

For Phase 2 Cohort 1 Arm A vs Arm B, PFS by investigator assessment will be analyzed using Kaplan-Meier (KM) methods. The KM estimate of the survival function will be computed, and the results will be presented using KM curves by treatment group. The median, Q1, Q3 will be provided along with the corresponding 95% confidence interval (CI) calculated by the Brookmeyer and Crowley method {Brookmeyer 1982}with log-log transformation. A log-rank test will be used to compare treatment difference in PFS by investigator.

In addition, the treatment effect will be estimated by hazard ratio along with its 2-sided 95% CI using the Cox proportional hazards regression model.

For Phase 2 Cohort 2 participants who are dosed at the selected Phase 2 Cohort 2 dose level, confirmed ORR by investigator assessment along with the 2-sided 95% exact CI based on the Clopper-Pearson method {Clopper 1934} will be summarized. Participants who do not have sufficient baseline or on-study tumor assessment to characterize response will be counted as nonresponders.

Efficacy analysis for Safety Run-in Cohorts will be listed only in the final analysis.

6.1.3. Sensitivity Analysis of the Primary Efficacy Endpoint

In order to evaluate the robustness of the primary endpoint of PFS by investigator assessment, sensitivity analysis will be performed with a different set of censoring rules. The censoring rules for primary and sensitivity analysis are summarized in Table 6-1.

Table 6-1. Censoring rule for primary and sensitivity analysis of PFS

Situation	Primary Analysis	Sensitivity Analysis 1
Documented Progressive Disease (PD)	Progressed at date of earliest sign of PD	Same as "Primary Analysis"
Death before first PD	Progressed at date of death	Same as "Primary Analysis"
Death within 2 disease assessments window and no baseline or post-baseline assessment	Progressed at date of death	Same as "Primary Analysis"
Alive and progression-free	Censored at date of last evaluable disease assessment	Same as "Primary Analysis"
Initiated subsequent anticancer therapy prior to PD or death	Censored at date of last evaluable assessment on or prior to subsequent anticancer therapy	Progressed at date of documented PD or death
PD or death immediately after ≥ 2 consecutively missed or not evaluable (NE) disease assessments	Censored at date of last evaluable assessment prior to missed or NE assessments	Progressed at date of documented PD or death
No disease assessment at baseline or post-baseline assessment	Censored at date of randomization (or first dosing date for non-randomized cohorts/phases)	Same as "Primary Analysis"

Given the scheduled visit assessment scheme,

- Cohort 1: Every 8 weeks (± 7 days) during the study
- Cohort 2: Every 6 weeks (± 7 days) through 36 weeks (Week 6, 12, 18, 24, 30, and 36) during the study, then every 9 weeks (± 7 days)

The definition of 2 missed visits will change. For Cohort 1, 2 missing visits are defined as 2 x (8 weeks + 7) days. For cohort 2, the 2 missing visits will be 2 x (6 weeks + 7) if the two missing visits occur before scheduled frequency of assessments changes, 2 x (9 weeks + 7) if the two missing visits occur after scheduled frequency of assessments changes, 6 weeks + 7 for an early assessment + 9 weeks + 7 for a late assessment if the two missed visits occur over the period when the scheduled frequency of assessments changes from every 6 weeks to every 9 weeks.

The sensitivity analysis of the primary efficacy endpoint will be removed in final analysis due to the program determination.

6.2. Secondary and CCI [redacted]

6.2.1. Definition of Secondary and CCI [redacted]

The secondary efficacy endpoints of this study include:

- Confirmed ORR per investigator assessment for Phase 2 Cohort 1
- PFS per investigator assessment for Cohort 2 (pooled Safety Run-in Cohort 2 and Phase 2 Cohort 2)
- DOR per investigator assessment for both Phase 2 Cohort 1 and Cohort 2 (pooled Safety Run-in Cohort 2 and Phase 2 Cohort 2)
- OS for both Phase 2 Cohort 1 and Cohort 2 (pooled Safety Run-in Cohort 2 and Phase 2 Cohort 2)

CCI [redacted]

Objective Response Rate (ORR) per investigator assessment for Phase 2 Cohort 1

ORR is defined as the proportion of patients who achieve the best overall response (BOR) of complete response (CR) or partial response (PR) that is confirmed at least 4 weeks after initial documentation of response, as determined by investigator assessment per RECIST, Version 1.1. 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 received new anticancer therapy prior to achieving CR or PR will be considered as non-responders.

PFS per investigator assessment for Cohort 2

For Cohort 2, PFS is defined as the time from the first dosing date of any study drug until the earliest date of first documented disease progression as determined based on response evaluation criteria in solid tumors (RECIST), Version 1.1, or death from any cause.

Overall Survival (OS)

Overall survival (OS) is defined as the interval from randomization date (Phase 2 Cohort 1) or the first dosing date (Safety Run-in Cohort 2 or Phase 2 Cohort 2) 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 will be censored at their last known alive date.

Duration of response (DOR) per investigator assessment

Defined as time from first documentation of complete response or partial response to the earliest date of the first documented disease progression as determined by investigator assessment, per RECIST Version 1.1, or death from any cause.

PRO endpoints measured by EORTC QLQ-C30 and EORTC-QLQ-BR23

The EORTC QLQ-C30 consists of 30 items, which address 15 HRQoL domains: 5 functional scales (physical functioning, role functioning, emotional functioning, cognitive functioning, and social functioning), 1 global health status scale, 3 symptom scales (fatigue, nausea and vomiting, and pain) and 6 single items (dyspnea, insomnia, loss of appetite, constipation, diarrhea, and financial difficulties){Fayers 2001} (See details in Appendix 2). The recall period is 1 week (past week). It will take about 11 minutes to complete. The accompanying module for breast cancer, EORTC-QLQ-BR23, has an additional 23 questions, which address 8 HRQoL domains: 4 functional scalses (Body image, Sexual functioning, Sexual enjoyment, Future perspective), 4 symptom scales (Systemic therapy side effects, Breast symptoms, Arm symptoms, Upset by hair loss).

According to the EORTC QLQ-C30 (EORTC-QLQ-BR23) Scoring Manual, scores for each scale (or domain) should be calculated if responses are given to at least 50% of the items in that particular scale; otherwise, it should be considered as missing. When there are multiple responses selected, the worst response will be selected for analysis.

For all scales, the raw score (RS) is defined as the mean of the non-missing component items (I_i): RS = (I_1 + I_2 +…+I_n)/n. For example, RS for emotional function is (Q_{21} + Q_{22} + Q_{24})/3 with missing data from Q_{23}. The standardized scores (S) are calculated as follows with range being defined as the difference between the maximum possible value of RS and the minimum possible value (e.g., most items are scored from 1 to 4, and therefore the range is equal to 3, except for Global health status/QoL with the range of 6 as from Table A2-1 and Table A3-1).

Functional scales: $S = (1 - \frac{RS - 1}{range}) \times 100$

Symptom scales and Global health status/QoL: $S = (\frac{RS - 1}{range}) \times 100$

All of the standardized scales and single-item measures range in score from 0 to 100. A high scale score represents a higher response level. Thus a high score for a functional scale represents a high / healthy level of functioning, a high score for the global health status / QoL represents a high QoL, but a high score for a symptom scale / item represents a high level of symptomatology / problems.

The scoring system for the QLQ-BR23 is identical in principle to that for the function and symptom scales and single items of the EORTC QLQ-C30 and each scale is transformed to provide a score ranging from 0 to 100 (Appendix 3). A high score for the functional scales indicates a high/healthy level of functioning, while a high score for the symptom scales indicates an elevated level of symptomatology or issues.

Change from baseline in each domain of EORTC QLQ-C30/EORTC-QLQ-BR23 will also be derived.

PRO endpoints measured by EQ-5D-5L

The EQ-5D-5L is an instrument for use as a measure of health outcome {EuroQol Research Foundation 2017, Janssen 2013}. The EQ-5D-5L consists of 2 sections: the EQ-5D descriptive system and the EQ visual analogue scale (EQ-VAS).

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

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

Change from baseline in EQ-VAS will also be derived.

6.2.2. Analysis Methods for Secondary and CCI [redacted]

Analysis of OS and DOR by investigator assessment for Phase 2 Cohort 1 and OS, DOR by investigator assessment and PFS by investigator assessment for Phase 2 Cohort 2 will be performed using the Kaplan-Meier method. Median, Q1, and Q3 will be derived based on KM estimates along with the corresponding 95% CI by the Brookmeyer and Crowley method with log-log transformation. Kaplan-Meier curves will be provided.

Confirmed ORR by investigator assessment for Phase 2 Cohort 1 along with the 95% CI will be estimated based on the Clopper-Pearson method for each treatment group. The chi-square test may be used to compare treatment difference in ORR. Odds ratios and corresponding 95% CIs will also be presented.

CCI [redacted]

[redacted]

6.3. Other Efficacy Definition and Analyses

6.3.1. Other Definition of Related to Efficacy

The PFS, ORR, DOR, OS for Safety Run-In Cohort 1 have the same definitions as those for Cohort 2.

Best objective response (BOR)

Best objective response (BOR) is calculated based on the overall visit responses from each RECIST assessment including unscheduled visits. It is the best response a patient has had from the start of treatment until objective documentation of PD (per RECIST v1.1), or patient withdrawn from the study, or patient started new anticancer therapy, whichever occurs first. Categorization of BOR will be based on RECIST v1.1 using the following response categories: CR, PR, SD, PD and NE.

A BOR of CR or PR must be confirmed. A BOR of CR/PR requires confirmation no less than 4 weeks (28 days) after the first response criterion was met and with no evidence of progression between the initial and CR/PR confirmation visit. Patients who responded with an unconfirmed CR/PR at the time of data cutoff will be reported as unconfirmed CR/PR under the SD category provided the minimum criteria for SD duration are met, otherwise this will be reported under the NE category.

For determination of a BOR of SD, the SD should be recorded at least 42 days after the first dosing date or randomization date (Phase 2 Cohort 1 only). For the determination of BOR, an overall visit response with “Non-CR/non-PD” is considered as SD.

6.3.2. Other Analysis Methods Related to Efficacy

The PFS, ORR, DOR, OS for Safety Run-in Cohorts will be listed only.

Best objective response (BOR)

For each treatment arm, best objective response (BOR) will be summarised by n (%) for each category (CR, PR, SD, PD and NE). No formal statistical analyses are planned for BOR.

6.4. Changes From Protocol-Specified Efficacy Analyses

Efficacy analyses for Safety Run-in Cohort 2 will be listed only for the purpose of synoptic CSR.

7. SAFETY ANALYSES

Safety analysis will be performed in the Safety Analysis Set. Listings will be based on the ITT analysis set for Phase 2 Cohort 1 and All Enrolled Analyses Set for Safety Run-in Cohorts and Phase 2 Cohort 2. Analysis of DLT was performed using the DLT-Evaluable Analysis Set for Safety Run-in evaluations.

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" for each study drug and overall. 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 safety 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 is the same as or after the month and year (or year) of the first dosing date of study drug, and
- The AE onset date is the same as or before the month and year (or year) of the date corresponding to the cutoff date of TEAE period, which is defined as the 30 days after the study drug last dose 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 or later month and year (or year alone if month is not recorded) as the first dosing date of study drug will be considered treatment emergent.

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

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

7.1.6. Summaries of DLTs, Adverse Events and Deaths

A brief, high-level summary of the number of percentage of patients who experienced at least 1 TEAE in the categories described below will be provided for each cohort and treatment group.

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

For the AE categories described below, summaries will be provided by SOC, PT, and cohort and treatment group:

- TEAEs
- TEAEs with Grade 3 or higher
- TE treatment-related AEs for magrolimab and for study drug other than magrolimab
- TE treatment-related AEs with Grade 3 or higher for magrolimab and for study drug other than magrolimab
- TE SAEs
- TE treatment-related SAEs for magrolimab and for study drug other than magrolimab
- TEAEs leading to dose reduction for study drug other than magrolimab
- TEAEs leading to dose delay or interruption for magrolimab and study drug other than magrolimab
- TEAEs leading to discontinuation of magrolimab and forstudy drug other than magrolimab
- TEAEs leading to death

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 within each SOC in the descending order of overall frequency. For summaries by severity, the most severe severity will be used for those AEs that occurred more than once in a given subject during the study.

In addition to the above summary tables, all TEAEs, TEAEs of Grade 3 or higher, TE SAEs will be summarized by PT only in descending order of overall frequencies.

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

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

A summary (number and percentage of patients) of deaths will be provided for each cohort and treatment group. 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. Treatment-Emergent Adverse Events (TEAE) 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 for each cohort and treatment group. Grade 3 or higher TEAE of clinical importance will be summarized by PT and severity.

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)
Myocardial Infarction	SMQ Myocardial infarction (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 during the treatment-emergent period. The analysis will be based on values reported in conventional units, unless specified otherwise.

7.2.1. Summaries of Numeric Laboratory Results

Descriptive statistics will be provided by cohort and treatment group for selected laboratory test specified in the study protocol as follows:

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

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

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 before 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 before 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 for each cohort and treatment group; 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)

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

For all summaries of laboratory abnormalities, the denominator is the number of patients in the the number of patients with nonmissing postbaseline values during treatment emergent period.

By-patients listings of all laboratory test results that were collected throughout the study for the laboratory test of interest will be provided for each cohort and treatment group, with flags for treatment-emergent laboratory abnormalities and treatment-emergent marked laboratory abnormalities. By-patient listing for post-infusion hematology will also be provided.

7.2.3. Liver-related Laboratory Evaluations

Liver-related abnormalities after the first dose of any study drug will be examined and summarized for each cohort and treatment group 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 during the treatment emergent period. 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 each cohort and treatment group for body weight, BMI, blood pressure, heart rate, temperature, and respiratory rate as follows:

- 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 date of first dose of any study drug (and prior to first dosing time if available).

A by-patient listing of vital signs will be provided by subject ID number and time point 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. Electrocardiogram Results

A by-patient listing of ECG results will be provided by subject ID number in ascending order for each cohort and treatment group.

7.5. Other Safety Measures

A by-patient listing of ECOG performance status will be provided by subject ID number in ascending order for each cohort and treatment group. A by-subject listing will be provided by subject ID number in ascending order for pregnancy test results.

7.6. Changes From Protocol-Specified Safety Analyses

In the final analysis, Safety Run-in Cohort 2 and Phase 2 Cohort 2 will be analyzed separately, while Safety Run-in Cohort 1 and Phase 2 Cohort 1 Arm A will be pooled.

8. CHANGES FROM PROTOCOL-SPECIFIED ANALYSES

Safety Run-in Cohort 2 and Phase 2 Cohort 2 will not be pooled in the final analysis. The efficacy analysis for Safety Run-in Cohort 2 will be listed only. Safety Run-in Cohort 1 and Phase 2 Cohort 1 Arm A will be pooled for the safety analysis in the final analysis.

9. PHARMACOKINETIC (PK) AND IMMUNOGENICITY ANALYSES

9.1. PK Analyses

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 time point and treatment arm/cohort.

9.2. Immunogenicity analysis

9.2.1. Definition of Terminology

Subjects Evaluable for ADA Prevalence: subjects who have at least one reportable ADA result at baseline or post-baseline.

Subjects Evaluable for ADA Incidence: subjects who have non-missing baseline ADA result and at least one reportable ADA result at post-baseline.

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

Treatment-Induced ADA Rate: the proportion of 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.

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.

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.

9.2.2. Evaluation of Immunogenicity Data

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

10. BIOMARKER ANALYSIS

Biomarker analysis will be described in a separate Biomarker Analysis Plan.

11. REFERENCES

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Lee JJ, Kuo Y-W, Liu D, Chen N. Bayesian Toxicity Monitoring. Available at: https://trialdesign.org/one-page-shell.html#BTOX Accessed: 23 January 2024. Last Updated: 22 April. 2021:

12. SOFTWARE

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

nQuery Advisor(R) Version 8.0. Statistical Solutions, Cork, Ireland.

EAST Version 6.5, Cytel Inc., MA, USA

13. SAP REVISION

Revision Date (DD MMM YYYY)	Section	Summary of Revision	Reason for Revision
13 Aug 2024	2.3	A sentence added to indicate that the primay analysis is canceled.	The primary analysis is canceled due to program decision.
13 Aug 2024	3.1.3	Replacing "pooled efficacy analysis for Safety Run-in Cohort 2 and Phase 2 Cohort 2" by "Phase 2 Cohort 2"	Safety Run-in Cohort 2 will be listed only for efficacy analysis.
13 Aug 2024	3.2.2.2	Adding a sentence "Due to the determination of the program, primary analysis is canceled."	The primary analysis is canceled due to program decision.
13 Aug 2024	3.2.2.3	Removing "For analyses to be performed at the final analysis, same grouping strategy as the primary analysis will be used." Adding "pooled Safety Run-in Cohort 1 and Phase 2 Cohort 1 Arm A" for safety analysis.	The primary analysis is canceled due to program decision. Safety Run-in Cohort 1 and Phase 2 Cohort 1 Arm A will be pooled for safety analysis.
13 Aug 2024	4, 5, 5.3, 6, 6.2.2	Replacing "(pooled safety run-in cohort 2 and phase 2 cohort 2)" by "Phase 2 Cohort 2"	Safety Run-in Cohort 2 will be listed only for efficacy analysis.
13 Aug 2024	6.1.2	Adding "Efficacy analysis for Safety Run-in Cohorts will be listed only in the final analysis."	Safety Run-in Cohorts will be listed only for efficacy analysis.
13 Aug 2024	6.1.3	Adding "The sensitivity analysis of the primary efficacy endpoint will be removed in final analysis due to the program determination."	The sensitivity analysis of the primary efficacy endpoint will not be summarized in the final analysis.
13 Aug 2024	6.2.1	Adding "PFS, DOR and OS for Safety Run-in Cohort 2 will be listed only for final analysis."	Safety Run-in Cohort 2 will be listed only for efficacy analysis.
13 Aug 2024	6.3.2	Changing to "The PFS, ORR, DOR, OS for Safety Run-in Cohorts will be listed only"	Safety Run-in Cohorts will be listed only for efficacy analysis.
13 Aug 2024	6.4	Changing to "Efficacy analyses for Safety Run-in Cohort 2 will be listed only for the purpose of synoptic CSR."	Safety Run-in Cohort 2 will be listed only for efficacy analysis.
13 Aug 2024	7	Replacing "(pooled safety run-in cohort 2 and phase 2 cohort 2)" by "Phase 2 Cohort 2"	Safety Run-in Cohort 2 and Phase 2 Cohort 2 will not be pooled for safety analysis.

13 Aug 2024	7.1.6	Replacing “to any study drug” by “Magrolimab and other study drug other than Magrolimab”	Magrolimab and other study drug other than Magrolimab will be summarized separately.
13 Aug 2024	7.1.7.1	Adding “Myocardial Infarction” in TEAE of Clinical Importance.	Adding TEAE of Clinical Importance per Patient Safety.
13 Aug 2024	8	Changing to “Safety Run-in Cohort 2 and Phase 2 Cohort 2 will not be pooled in the final analysis. The efficacy analysis for Safety Run-in Cohort 2 will be listed only.”	Safety Run-in Cohort 2 will be listed only for efficacy analysis.

14. APPENDICES

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 A1-1 summarizes overall visit responses given the visit responses from TL and NTL are combined with new leision.

Table A1-1. 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	NE

CR Complete response, NA Not applicable, PR Partial response, SD Stable disease, PD Progression of disease, NE Not evaluable.

Appendix 2 Overview of EORTC QLQ-C30 Questionnaire

The EORTC QLQ-C30 is a well-validated questionnaire commonly used in oncology trials. It consists of 30 items, which address 15 HRQoL domains: five multi-item functional scales, three multi-item symptom scales, a global health status/QoL scale, and six single-item symptom scales (Table A2-1).

Table A2-1. Overview of EORTC QLQ-C30 (Version 3)

EORTC QLQ-C30 Domains	Number of Items	Item Range*	Item Numbers (Version 3)
Global health status/QoL	2	1–7	29, 30
Functional Domains			
Physical functioning	5	1–4	1–5
Role functioning	2	1–4	6, 7
Emotional functioning	4	1–4	21–24
Cognitive functioning	2	1–4	20, 25
Social functioning	2	1–4	26, 27
Symptom and Financial Difficulty Domains			
Fatigue	3	1–4	10, 12, 18
Nausea and vomiting	2	1–4	14, 15
Pain	2	1–4	9, 19
Dyspnea	1	1–4	8
Insomnia	1	1–4	11
Appetite loss	1	1–4	13
Constipation	1	1–4	16
Diarrhea	1	1–4	17
Financial difficulties	1	1–4	28

Abbreviations: EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Core 30 Questionnaire; QoL = quality of life
* Item range is the difference between the possible maximum and the minimum response to individual items; range=3 for items taking value from 1 to 4; range=6 for iterms taking value from 1 to 7.

ENGLISH

EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials:
Your birthdate (Day, Month, Year):
Today's date (Day, Month, Year): 31

	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a long walk?	1	2	3	4
3. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:

	Not at All	A Little	Quite a Bit	Very Much
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4

Please go on to the next page

ENGLISH

During the past week:	Not at All	A Little	Quite a Bit	Very Much
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall quality of life during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

Appendix 3 Overview of EORTC QLQ-BR23 Questionnaire

Table A3-1. Overview of EORTC QLQ-BR23

EORTC QLQ-BR23 Domains	Number of Items	Item Range*	Item Numbers (Version 3)	†
Functional scales				
Body Imaging	4	1–4	9-12	F
Sexual Functioning	2	1–4	14, 15	†
Sexual enjoyment	1	1–4	16	†
Future perspective	1	1–4	13	F
Symptom scales/items				
Systemic therapy side effects	7	1–4	1-4, 6,7,8	
Breast symptoms	4	1–4	20-23	
Arm symptoms	3	1–4	17, 18,19	
Upset by hair loss	1	1–4	5	

Abbreviations: EORTC QLQ-BR23 = European Organisation for Research and Treatment of Cancer Quality of Life Breast Cancer module 23 Questionnaire; QoL = quality of life
* Item range is the difference between the possible maximum and the minimum response to individual items; range=3 for items taking value from 1 to 4.
† Items for the scales marked † are scored positively (i.e. “very much” is best) and therefore use the same algebraic equation as for symptom scales; however, the Body Image scale uses the algebraic equation for functioning scales.

EORTC QLQ - BR23

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week.

During the past week:	Not at All	A Little	Quite a Bit	Very Much
31. Did you have a dry mouth?	1	2	3	4
32. Did food and drink taste different than usual?	1	2	3	4
33. Were your eyes painful, irritated or watery?	1	2	3	4
34. Have you lost any hair?	1	2	3	4
35. Answer this question only if you had any hair loss: Were you upset by the loss of your hair?	1	2	3	4
36. Did you feel ill or unwell?	1	2	3	4
37. Did you have hot flushes?	1	2	3	4
38. Did you have headaches?	1	2	3	4
39. Have you felt physically less attractive as a result of your disease or treatment?	1	2	3	4
40. Have you been feeling less feminine as a result of your disease or treatment?	1	2	3	4
41. Did you find it difficult to look at yourself naked?	1	2	3	4
42. Have you been dissatisfied with your body?	1	2	3	4
43. Were you worried about your health in the future?	1	2	3	4

During the past four weeks:	Not at All	A Little	Quite a Bit	Very Much
44. To what extent were you interested in sex?	1	2	3	4
45. To what extent were you sexually active? (with or without intercourse)	1	2	3	4
46. Answer this question only if you have been sexually active: To what extent was sex enjoyable for you?	1	2	3	4

During the past week:	**Not at All**	**A Little**	**Quite a Bit**	**Very Much**
47. Did you have any pain in your arm or shoulder?	1	2	3	4
48. Did you have a swollen arm or hand?	1	2	3	4
49. Was it difficult to raise your arm or to move it sideways?	1	2	3	4
50. Have you had any pain in the area of your affected breast?	1	2	3	4
51. Was the area of your affected breast swollen?	1	2	3	4
52. Was the area of your affected breast oversensitive?	1	2	3	4
53. Have you had skin problems on or in the area of your affected breast (e.g., itchy, dry, flaky)?	1	2	3	4

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ELECTRONIC SIGNATURES

Signed by	Meaning of Signature	Server Date (dd-MMM-yyyy hh:mm:ss)
Xuan Liu14	Biostatistics eSigned	06-Sep-2024 21:32:33
Yehong Wang22	Clinical Pharmacology eSigned	06-Sep-2024 21:43:13
Michael Howland	Early Development Lead (EDL) eSigned	09-Sep-2024 16:23:40