STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 1b/2 Trial of Hu5F9-G4 in Combination with Rituximab or Rituximab + Chemotherapy in Patients with Relapsed/Refractory B-cell Non-Hodgkin's Lymphoma
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CONFIDENTIAL AND PROPRIETARY INFORMATION

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LIST OF ABBREVIATIONS

ADA	antidrug antibody
AE	adverse event
ALT	alanine aminotransferase
aPTT	activated partial thromboplastin time
ASCT	autologous stem cell transplant
AST	aspartate aminotransferase
AUC	area under the concentration-time curve
BLQ	below the limit of quantitation
BMI	body mass index
CFR	Code of Federal Regulations
CI	confidence interval
CK	creatine kinase
C_{max}	maximum serum concentration
COVID-19	Coronavirus disease 2019
CR	complete response
CRF	case report form
CSR	clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
CTSC	Clinical Trial Steering Committee
CyTOF	mass cytometry
DILI	drug-induced liver injury
DLBCL	diffuse large B-cell lymphoma
DLT	dose-limiting toxicity
DNA	deoxyribonucleic acidi
DOR	duration of response
DMC	data monitoring committee
EAS	Efficacy Analysis Set
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic case report form
ET	early termination
Hb	hemoglobin
HLT	high-level term
ICH	International Conference on Harmonization (of Technical Requirements for Registration of Pharmaceuticals for Human Use)
IL	Indolent lymphoma
INR	international normalized ratio
ITT	intent to treat
KM	Kaplan-Meier

LLT	lower-level term
LOQ	limit of quantitation
LYRIC	Lymphoma Response to Immunomodulatory therapy Criteria
MDS	myelodysplastic syndrome
MedDRA	Medical Dictionary for Regulatory Activities
MMDL	median maintenance dose level
MST	MedDRA Search Term
MTD	maximum tolerable dose
NCI-CTCAE	National Cancer Institute Common-Terminology Criteria for Adverse Events
NHL	non-Hodgkin's lymphoma
NLP	natural language processing
ORR	objective response rate
OS	overall survival
PP	per protocol
PFS	progression-free survival
PK	pharmacokinetic
PR	partial response
PT	preferred term
Q1, Q3	first quartile, third quartile
Q2W	every two weeks
QRS	electrocardiographic deflection between the beginning of the Q wave and termination of the S wave representing time for ventricular depolarization
QT	electrocardiographic interval between the beginning of the Q wave and termination of the T wave representing the time for both ventricular depolarization and repolarization to occur
QTc	QT interval corrected for heart rate
QTcF	QT interval corrected for heart rate using Fridericia's formula
RBC	red blood cells
R-GemOx	rituximab, gemcitabine, and oxaliplatin
RO	receptor occupancy
RP2DS	recommended Phase 2 dose and schedule
RR	electrocardiographic interval representing the time measurement between the R wave of one heartbeat and the R wave of the preceding heartbeat
SAF	Safety Analysis Set
SAP	statistical analysis plan
SD	standard deviation
SI (units)	international system of units
SMQ	Standardised MedDRA Queries
SOC	system organ class
TEAE	treatment-emergent adverse event
TFLs	tables, figures, and listings
TTP	time to progression

ULN	upper limit of normal
VR	ventricular rate
WBC	white blood cells
WHO	World Health Organization

1. INTRODUCTION

This statistical analysis plan (SAP) describes the statistical analysis methods and data presentations to be used in tables, figures, and listings (TFLs) of the final analysis for Study 5F9003. The purpose of this final analysis is to summarize the available safety and efficacy data from Study 5F9003 for the final synoptic CSR.

The SAP is based on the 5F9003 Study Protocol Amendment 12 dated 02 November 2023 and the electronic case report form (eCRF). The SAP will be finalized prior to data finalization for the final analysis. Any changes made after the finalization of the SAP will be documented in the clinical study report (CSR).

1.1. Study Objectives

PRIMARY	
Objectives	**Endpoints**
• To investigate the safety and tolerability, and to define the RP2DS for magrolimab in combination with rituximab and for magrolimab in combination with R-GemOx • To evaluate the efficacy of magrolimab in combination with rituximab in patients with indolent lymphoma and DLBCL and to evaluate the efficacy of magrolimab in combination with R-GemOx in autologous stem cell transplant (ASCT) ineligible DLBCL as measured by the ORR according to Lugano Classification for lymphomas {Cheson 2014}	• Dose-limiting toxicities (DLTs) (Phase 1b only [in the antibody combination (magrolimab + rituximab) and the chemotherapy combination (magrolimab + R-GemOX) cohorts]) and adverse events (AEs) according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), Version 4.03 • ORR as defined by the Investigator according to the Lugano Classification for lymphomas

SECONDARY

Objectives	Endpoints
• To evaluate the pharmacokinetic (PK) profiles of magrolimab in combination with rituximab and magrolimab in combination with R-GemOx • To evaluate the immunogenicity of magrolimab in combination with rituximab and magrolimab in combination with R-GemOx • To evaluate the efficacy of magrolimab in combination with rituximab in indolent lymphoma and DLBCL, and magrolimab in combination with R-GemOx in ASCT ineligible DLBCL as measured by the duration of response (DOR), progression-free survival (PFS), overall survival (OS), and time to progression (TTP) • To evaluate the efficacy of magrolimab in combination with rituximab in patients with indolent lymphoma and DLBCL, and magrolimab in combination with R-GemOx in ASCT ineligible DLBCL as measured by ORR according to Lymphoma Response to Immunomodulatory therapy Criteria (LYRIC; {Cheson 2016})	• Concentration versus time measurements for magrolimab in combination with rituximab and for magrolimab in combination with R-GemOx and their PK parameters including maximum serum concentration (C_{max}), and area under the concentration time curve (AUC) • Anti-drug antibodies (ADA) to magrolimab in combination with rituximab and magrolimab in combination with R-GemOx • DOR, PFS, OS, and TTP • ORR as defined by the Investigator according to the LYRIC Criteria for lymphomas

1.2. Study Design

This is an open-label, multicenter, Phase 1b/2 trial investigating the combination of magrolimab + rituximab (antibody combination) and R-GemOx (chemotherapy combination) in R/R B-cell NHL. Safety and tolerability will be investigated during the Phase 1b portion of the study to determine the MTD and define a recommended phase 2 dose schedule (RP2DS) for magrolimab + rituximab and magrolimab + R-GemOx. The primary efficacy analysis will be evaluated using the R2PDS in the Phase 2 portion of the study on the objective response rate (ORR) as defined by the investigator in accordance with the Lugano Classification {Cheson 2014}. Additional analyses will be performed to better understand the PK, immunogenicity, duration of response, progression-free survival, overall survival, and time to progression.

Further details of the study, including the schedule of assessments, are described in 5F9003 Study Protocol Amendment 12.

1.2.1. Key Inclusion Criteria

1) Antibody combination (magrolimab + rituximab) Phase 1b cohort only: B-cell NHL expressing CD20 by immunohistochemistry (IHC) or flow cytometry, relapsed or refractory to at least 2 prior lines of therapy.

2) Diffuse large B-cell lymphoma (DLBCL) chemotherapy combination (magrolimab + R-GemOx) Phase 1b safety dose-escalation and expansion cohorts:

   a) Histologically confirmed de novo or transformed DLBCL relapsed or refractory to 1 to 3 prior lines of therapy who are not candidates for high-dose chemotherapy and autologous stem cell transplantation (ASCT). Patients relapsed after ASCT are allowed.

   b) At least 1 prior therapy must have included a CD20-targeted therapy.

   c) Primary refractory patients are excluded as defined by failure to achieve a partial response (PR) or complete response (CR) to frontline therapy or progression within 3 months of completing treatment.

   d) The 1 to 3 prior lines of therapy requirement is only applicable for treatment regimens for DLBCL and not for prior lymphomas in the case of transformed DLBCL.

3) For the DLBCL antibody combination (magrolimab + rituximab) Phase 2 Cohort 4, de novo or transformed DLBCL, not otherwise specified, according to the World Health Organization 2016 classification of lymphoid neoplasms {Swerdlow 2016} expressing CD20 by IHC or flow cytometry, that is relapsed or refractory to at least 2 prior lines of therapy containing and anti-CD20 therapy. Prior autologous hematopoietic cell transplantation is permitted.

4) Indolent lymphoma Phase 2 Cohort: Histologically confirmed marginal zone or follicular lymphoma (Grade 1 to 3a) expressing CD20 by IHC or flow cytometry, relapsed or refractory to at least 2 prior lines of therapy.

5) Eastern Cooperative Oncology Group (ECOG) score 0 to 2

6) Disease that is measurable or assessable for response per Lugano Classification for lymphomas {Cheson 2014}

7) CAR-T naïve or CAR-T ineligible patients and otherwise meet other inclusion/exclusion criteria may enroll. Patients who relapse following CAR-T therapy are not eligible.

1.2.2. Key Exclusion Criteria

1) Prior allogeneic stem cell transplant

2) Prior anticancer therapy, including chemotherapy, hormonal therapy, and investigational agents within 3 weeks or within at least 4 half-lives prior to magrolimab dosing (up to a maximum of 4 weeks), whichever is longer.

3) Red blood cell (RBC) transfusion dependence, defined as requiring more than 2 units of RBC transfusions during the 4-week period prior to screening. RBC transfusions are permitted during screening and prior to enrollment to meet the hemoglobin inclusion criteria.

4) Additional exclusion criteria for DLBCL chemotherapy combination (magrolimab + R-GemOx) Phase 1b safety dose-escalation and expansion cohorts only:

   a) Undergone ASCT within a period of ≤ 3 months before signing informed consent.

   b) Prior treatment with gemcitabine and oxaliplatin. However, patients who relapse ≥ 12 months after treatment with a gemcitabine and oxaliplatin containing regimen are allowed.

   c) Known hypersensitivity to gemcitabine, oxaliplatin, or other platinum compounds.

   d) Intolerance of gemcitabine, oxaliplatin, and/or rituximab as monotherapy or in combination due to unacceptable toxicities as determined by the treating Investigator.

1.2.3. Phase 1b Antibody (Magrolimab + Rituximab) Study Design

Dose escalation for the Phase 1b antibody combination followed a standard 3 + 3 design in patients with B-cell NHL receiving magrolimab + rituximab to investigate a 1 mg/kg magrolimab priming dose followed by weekly maintenance doses of 10, 20, 30, or 45 mg/kg to determine the MTD and to identify the RP2DS for magrolimab in combination with rituximab. Rituximab was administered by IV infusion at the clinical approved dose of 375 mg/m^2. Magrolimab + rituximab treatment could have continued until loss of clinical benefit or unacceptable toxicity for patients who do not have disease progression. The detailed dosing regimens implemented in the Phase 1b antibody combination are described in Table 1.

Table 1. 5F9003: Antibody Combination (Magrolimab + Rituximab) Phase 1b Cohorts and Schedule

Cohort	Drug/Dose (Intravenous)		Dose Schedule (Day per 28-day Cycle)[a]		
			Cycle 1	Cycle 2	Cycle 3+
Phase 1b 1	Priming	Magrolimab 1 mg/kg	Day 1	—	—
	Maintenance	Magrolimab 10 mg/kg[a]	Day 8, 15, 22	Day 1, 8, 15, 22	Day 1, 8, 15, 22
		Rituximab 375 mg/m^2	Day 8, 15, 22	Day 1	C3-C6 Day 1
Phase 1b 2	Priming	Magrolimab 1 mg/kg	Day 1	—	—
	Maintenance	Magrolimab 20 mg/kg[a]	Day 8, 15, 22	Day 1, 8, 15, 22	Day 1, 8, 15, 22
		Rituximab 375 mg/m^2	Day 8, 15, 22	Day 1	C3-C6 Day 1
Phase 1b 3	Priming	Magrolimab 1 mg/kg	Day 1	—	—
	Maintenance	Magrolimab 30 mg/kg[a]	Day 8, 11[b], 15, 22	Day 1, 8, 15, 22	Day 1, 8, 15, 22
		Rituximab 375 mg/m^2	Day 8, 15, 22	Day 1	C3-C6 Day 1
Phase 1b 4	Priming	Magrolimab 1 mg/kg	Day 1	—	—
	Maintenance	Magrolimab 45 mg/kg[a]	Day 8, 11[b], 15, 22	Day 1, 8, 15, 22	Day 1, 15
		Rituximab 375 mg/m^2	Day 8, 15, 22	Day 1	C3-C6 Day 1

C = cycle number; RP2DS = recommended Phase 2 dose and schedule

a Phase 1b patients who continued treatment in Phase 2 could have followed the Phase 2 dosing schedule (ie, at the RP2DS). In Protocol Amendment 6, rituximab dosing was added to Day 1 of every other cycle starting with Cycle 8 and continuing beyond.

b A loading dose of magrolimab was administered on Cycle 1 Day 11 for the loading dose cohort.

Based on review of Phase 1b cohort data, the Clinical Trial Steering Committee (CTSC) determined the magrolimab RP2DS to be 1 mg/kg priming dose, followed by 30 mg/kg maintenance IV weekly dose during Cycle 1, and then every two weeks (Q2W) starting at Cycle 2 (cycle length is 28 days).

1.2.4. Phase 2 Antibody (Magrolimab + Rituximab) Study Design

The Phase 2 portion of the study initially explored the RP2DS determined from the Phase 1b antibody combination (magrolimab + rituximab) portion of the study. Additional dosing regimens were later explored resulting in a total of 4 Phase 2 cohorts as follows:

Table 2. 5F9003: Antibody Combination (Magrolimab + Rituximab) Phase 2 Cohorts and Schedule

Cohort	Drug/Dose (Intravenous)		Dose Schedule (Day per 28-day Cycle)			
			Cycle 1	Cycle 2	Cycles 3-6	Cycle 7+
Phase 2 1	Priming	Magrolimab 1 mg/kg	Day 1		—	—
	Maintenance	Magrolimab 30 mg/kg	Day 8, 15, 22	Day 1, 15	Day 1, 15	Day 1, 15
		Rituximab 375 mg/m^2	Day 8, 15, 22	Day 1	Day 1	Day 1 every other cycle starting at Cycle 8
Phase 2 2	Priming	Magrolimab 1 mg/kg	Day 1		—	—
	Maintenance	Magrolimab 30 mg/kg	Day 8, 11[a] 15, 22	Day 1, 8, 15, 22	Day 1, 15	Day 1, 15
		Rituximab 375 mg/m^2	Day 8, 15, 22	Day 1	Day 1	Day 1 every other cycle starting at Cycle 8
Phase 2 3	Priming	Magrolimab 1 mg/kg	Day 1		—	—
	Maintenance	Magrolimab 45 mg/kg	Day 8, 11[a], 15, 22	Day 1, 8, 15, 22	Day 1, 15	Day 1, 15
		Rituximab 375 mg/m^2	Day 8, 15, 22	Day 1	Day 1	Day 1 every other cycle starting at Cycle 8
Phase 2 4 (DLBCL only)	Priming	Magrolimab 1 mg/kg	Day 1	—	—	—
	Maintenance	Magrolimab 30 mg/kg[b]	Day 8[b], 15, 22	Day 1, 8, 15, 22	Day 1, 15	Day 1, 15
		Rituximab 375 mg/m^2 [b]	Day 8[b], 15, 22	Day 1	C6 Day 1	Day 1 every other cycle starting at Cycle 8

C = cycle number; DLBCL = diffuse large B-cell lymphoma
a A loading dose of magrolimab was administered on Cycle 1 Day 11.
b On Cycle 1 Day 8, magrolimab was administered first, followed by rituximab at least 1 hour later. For all other times when rituximab and magrolimab were administered at the same visit, rituximab was administered first. There was at least an hour interval between the end of infusion of the first drug and the beginning of the infusion of the second drug.

- Phase 2 Cohort 1 (RP2DS) : Magrolimab 1 mg/kg (prime), Magrolimab 30 mg/kg (maintenance) weekly during Cycle 1 then Q2W starting at Cycle 2 (cycle length is 28 days), and Rituximab 375 mg/m^2
- Phase 2 Cohort 2 : Magrolimab 1 mg/kg (prime), Magrolimab 30 mg/kg (loading dose on Cycle 1 Day 11), Magrolimab 30 mg/kg (maintenance) weekly through Cycle 2, then Q2W starting at Cycle 3, and Rituximab 375 mg/m^2

- Phase 2 Cohort 3 : Magrolimab 1 mg/kg (prime), Magrolimab 45 mg/kg (loading dose on Cycle 1 Day 11), Magrolimab 45 mg/kg (maintenance) weekly in Cycle 1 and 2, then Q2W starting at Cycle 3, and Rituximab 375 mg/m^2

- Phase 2 Cohort 4 (DLBCL only) : Magrolimab 1 mg/kg (prime), Magrolimab 30 mg/kg (maintenance) weekly through Cycle 2, then Q2W starting at Cycle 3, and Rituximab 375 mg/m^2

Magrolimab + rituximab treatment could have continued until loss of clinical benefit or unacceptable toxicity for patients who do not have disease progression. Details of the dosing regimens for each of the 4 Phase 2 cohorts are described in Table 2.

Enrollment in the initial RP2DS Phase 2 cohort 1 was conducted according to a 2-stage design, separately by tumor type (DLBCL and IL):

1) After 14 DLBCL or IL patients are enrolled in Phase 2 cohort 1 and have completed a 4-week safety assessment, an initial interim safety and efficacy analysis will be performed for those patients. Enrollment will continue only if < 33% of patients experience any Grade 3 or greater AE that is assessed as related to study drug (magrolimab and/or rituximab), and results in permanent discontinuation, withdrawal, or death, and only if ≥ 3 out of 14 patients achieve an objective response.

2) A subsequent interim efficacy analysis will be peformed for the DLBCL patients, after 40 efficacy-evaluable DLBCL patients have been enrolled. Enrollment will continue up to 94 DLBCL patients only if the observed response rate is ≥ 20%. A subsequent interim efficacy analysis will be peformed for the IL patients, after 24 efficacy-evaluable IL patients have been enrolled. Enrollment will continue up to 94 IL patients only if the ORR is ≥ 30% or if the CR rate is ≥ 20%.

After initial interim analyses of Phase 2 Cohort 1, the CTSC decided to explore additional dose regimens different from the RP2DS and enrolled 3 additional Phase 2 cohorts (Phase 2 Cohorts 2-4). Per 5F9003 Study Protocol Amendment 10, for Phase 2 Cohort 4, which enrolled only DLBCL patients, an interim safety and efficacy analysis was planned after 20 efficacy-evaluable patients have been enrolled, and further enrollment will continue only if the ORR is ≥ 20%.

1.2.5. Phase 1b Chemotherapy (Magrolimab + R-GemOx) Study Design

The combination of magrolimab + R-GemOx was explored in a Phase 1b study following a standard 3+3 design with an initial safety dose-escalation phase (with dose de-escalation if necessary) followed by an expansion phase (up to 20 additional patients) in high-dose chemotherapy/ASCT ineligible patients. Gemcitabine and oxaliplatin dosing are intended to complete after Cycle 4; however, dosing may continue beyond Cycle 4, as needed, until a total of 8 doses have been received at the discretion of the investigator. The detail dosing regimens are described in Table 3.

Table 3. 5F9003: Chemotherapy Combination (Magrolimab + R-GemOx) Safety Dose-Escalation and Expansion Phase Cohorts and Schedule

Cohort	Drug	Cycle 1 (5 weeks)	Cycle 2 (4 weeks)	Cycles 3–4 (4 weeks)	Cycles 5–6 (4 weeks)	Cycle 7+ (4 weeks)
Phase 1b 5	Dose escalation Magrolimab (IV)[a]	1 mg/kg priming: Day 1 30 mg/kg maintenance: Day 8, 11[b], 15, 22, 29	30 mg/kg maintenance: Day 1, 8, 15, 22	30 mg/kg maintenance: Day 1, 15	30 mg/kg maintenance: Day 1, 15	30 mg/kg maintenance: Day 1, 15
Phase 1b 6	Dose escalation Magrolimab (IV)[c]	1 mg/kg priming: Day 1 45 mg/kg maintenance: Day 8[i], 11[b], 15, 22, 29	45 mg/kg maintenance: Day 1, 8, 15, 22	45 mg/kg maintenance: Day 1, 15	45 mg/kg maintenance: Day 1, 15	45 mg/kg maintenance: Day 1, 15
Phase 1b 5[d]	Dose expansion Magrolimab (IV)[e]	1 mg/kg priming: Day 1 30 mg/kg maintenance: Day 8, 11[b,f], 15, 22, 29	30 mg/kg maintenance: Day 1, 8, 15, 22	30 mg/kg maintenance: Day 1, 15	30 mg/kg maintenance: Day 1, 15	30 mg/kg maintenance: Day 1, 15
Used for each cohort	Rituximab (IV)	375 mg/m^2: Day 8[i], 15, 22, 29	375 mg/m^2: Day 1	375 mg/m^2: Day 1	375 mg/m^2: Day 1 then Day 1 every other cycle starting Cycle 8	
	Gemcitabine (IV)	1000 mg/m^2: Day 11, 23	1000 mg/m^2: Day 2, 15	1000 mg/m^2: Day 2, 15	–	–
	Oxaliplatin (IV)	100 mg/m^2: Day 11, 23	100 mg/m^2: Day 2, 15	100 mg/m^2: Day 2, 15	–	–
	G-CSF prophylaxis[g]	Administer	Administer	Administer	–	–
	Allopurinol (oral)[h]	Daily	–	–	–	–

CTSC = Clinical Trial Steering Committee; G-CSF = granulocyte colony stimulating factor; IV = intravenous; MTD = maximum tolerated dose; Q2 months = every 2 months; R-GemOx = rituximab, gemcitabine, and oxaliplatin

a Magrolimab maintenance dose could have been de-escalated to 20 mg/kg or 10 mg/kg with the identical dosing schedule of maintenance doses if the regimen was deemed too toxic by the CTSC.

b A loading dose of magrolimab was administered on Cycle 1 Day 11.

c The CTSC could have decided to explore higher doses of magrolimab in increments up to 50% higher than the prior dose level deemed to be safe in accordance with the modified 3 + 3 design.

d Patients were enrolled into the same cohort as the 30 mg/kg magrolimab dose-escalation cohort.

e The magrolimab maintenance dose level utilized in the expansion phase was the recommended dose selected by the CTSC from the safety dose-escalation phase.

f The requirement for a loading dose of magrolimab on Cycle 1 Day 11 was removed in Protocol Amendment 10.

g G-CSF primary prophylaxis must be administered with gemcitabine and oxaliplatin treatment. Local standard of care or equivalent was to be administered in accordance with local institutional guidelines or investigator guidance. G-CSF prophylaxis should have generally occurred within several days after administration on each day that gemcitabine and oxaliplatin was dosed. However, the timing of G-CSF prophylaxis could have been given in accordance with local institutional guidelines.

h Allopurinol of 300 mg oral daily should have been administered for the first cycle only to prevent tumor lysis syndrome associated with chemotherapy. Allopurinol could have been given at 100 mg oral daily for the first cycle if significant renal impairment was present as determined by the investigator.
i On Cycle 1 Day 8 magrolimab is to be given first, followed by rituximab. For all other times when rituximab and magrolimab are given on the same visit, rituximab should be given first. There should be at least an hour interval between the end of infusion of the first drug and the beginning of the infusion of the second drug.

1.3. Sample Size and Power

The overall sample size planned for both the antibody combination (magrolimab + rituximab) and chemotherapy combination (magrolimab + R-GemOx) cohorts is up to 422 patients.

1.3.1. Phase 1b Antibody Combination (Magrolimab + Rituximab) Sample Size

For the antibody combination (magrolimab + rituximab), up to 354 patients were planned for enrollment in both the Phase 1b and Phase 2 parts. In the Phase 1b antibody combination (magrolimab + rituximab) cohort of the study, a standard 3 + 3 dose escalation design is employed to explore the MTD of the investigational combination. There were 4 dose cohort levels, with an estimated total of 25 to 38 patients planned in the Phase 1b depending on the possible cohort expansion in a 3 + 3 design.

1.3.2. Phase 2 Antibody Combination (Magrolimab + Rituximab) Sample Size

The Phase 2 part of the study will enroll patients with indolent lymphoma or DLBCL. Pending decisions from CTSC, additional arms in Phase 2 may be opened to test dose levels different from the current RP2DS of 30 mg/kg. Cohorts 1 to 3 of the antibody combination (magrolimab + rituximab) Phase 2 part of the study will comprise up to 216 patients evaluable for efficacy (up to 94 with indolent lymphoma and 94 with DLBCL) if both stages of each group are fully accrued. The additional 28 patients account for testing of additional dose regimens for indolent lymphoma and DLBCL. The sample size of 94 was determined to ensure the lower bound of the 95% CI will exclude 30% if the observed response rate is 40% or higher.

Cohort 4 of the antibody combination (magrolimab + rituximab) Phase 2 part of the study will comprise up to 100 DLBCL patients if both stages are fully accrued. The sample size of 100 was determined to ensure the lower bound of the 95% CI will exclude 20% if the ORR is 30% or higher. This desired ORR is based on a ORR that is higher than current standard of care and that provides significant clinical benefit for these DLBCL and indolent lymphoma heavily pretreated patient populations.

1.3.3. Phase 1b Chemotherapy Combination (Magrolimab + R-GemOx) Sample Size

For the chemotherapy combination (magrolimab + R-GemOx), the total planned number of patients for Phase 1b cohort was 29 to 68 efficacy-evaluable patients, including a safety dose escalation cohort of approximately 9 to 48 patients (if dose de-escalation occurs an additional 6 patients may be enrolled for 2 dose levels) and a dose expansion cohort of approximately 20 patients. The sample size of 26 total efficacy-evaluable patients at the selected dose level was calculated based on a desired ORR of ≥ 50% for the treatment combination. With a sample size

of 26 patients, the lower bound of the 95% CI would exclude an alternative ORR of 33%. A 33% ORR is what has been reported for R-GemOx in the indicated DLBCL population {Mounier 2013} with a desired ORR of ≥ 50% in the chemotherapy combination (magrolimab + R-GemOx) Phase 1b cohort is expected to provide a meaningful clinical improvement and benefit in this patient population.

2. TYPE OF PLANNED ANALYSIS

2.1. Interim Analyses

Interim analyses of safety and efficacy data generated during the trial were reviewed by the CTSC to make decisions about patient recruitment, trial management, initiation of protocol specific amendments, expansion of cohorts, using higher or lower dose levels, defining any new dose cohorts, identification of the RP2DS, and interim efficacy analysis decisions. A representative from the Sponsor, usually the Study Medical Monitor or designee, will chair the CTSC. The CTSC will oversee the conduct of the clinical trial and have representation from each participating site in the study. The CTSC will meet at a minimum at the completion of each dosing cohort during dose-escalation phase of the trial, at any protocol-specified formal interim analyses, and when emergent critical safety data are reported. The composition, structure, and function of the CTSC are defined in the CTSC Charter.

2.1.1. Planned Interim Analyses for Phase 1b Dose Escalation Cohorts

Interim analysis of on-going data for each Phase 1b cohort was reviewed by the CTSC based on the first 4 weeks of treatment in each cohort, referred to as the "Dose-Limiting Toxicity (DLT) Assessment Period," in conjunction with ongoing assessments for patients on prior cohorts who continued therapy beyond 4 weeks.

This includes analyses of the Phase 1b, Antibody combination cohorts:

- Phase 1b Cohort 1 : 5F9 10 mg/kg no load + Rituximab 375 mg/m^2
- Phase 1b Cohort 2 : 5F9 20 mg/kg no load + Rituximab 375 mg/m^2
- Phase 1b Cohort 3 : 5F9 30 mg/kg load + Rituximab 375 mg/m^2
- Phase 1b Cohort 4 : 5F9 45 mg/kg load + Rituximab 375 mg/m^2

And analysis of the Phase 1b, Chemotherapy combination cohorts:

- Phase 1b Cohort 5 : 5F9 30 mg/kg load + Rituximab 375 mg/m^2 + Gemcitabine 1000 mg/m^2 + Oxaliplatin 100 mg/m^2
- Phase 1b Cohort 6 : 5F9 45 mg/kg load + Rituximab 375 mg/m^2 + Gemcitabine 1000 mg/m^2 + Oxaliplatin 100 mg/m^2

Dose escalation analyses for Phase 1b Cohorts 1, 2, 3, 4, 5 and 6 have been completed and reviewed by the CTSC. Dose expansion analyses for the chemotherapy combination will occur when 26 total patients (up to 6 patients from the dose escalation phase, and at least 20 patients for the dose expansion phase) are evaluable for efficacy.

2.1.2. Planned Interim Analyses for Phase 2 Cohorts

Interim safety and efficacy analyses will be performed separately for DLBCL and IL patients treated with the RP2DS antibody combination enrolled in Phase 2 Cohort 1, and will be reviewed by the CTSC to decide whether to continue or stop enrollment after 14 efficacy-evaluable patients are available, respectively. If enrollment is approved, a subsequent interim analysis will be performed on the DLBCL patients in Phase 2 Cohort 1 when 40 efficacy-evaluable DLBCL patients are available, and a subsequent interim analysis will be performed on the IL patients in Phase 2 Cohort 1 when 24 efficacy-evaluable IL patients are available to determine whether to proceed to full accrual of 94 patients each for DL and IL patients, respectively. The initial interim safety and efficacy analyses of 14 efficacy-evaluable DLBCL and IL patients were completed and reviewed by the CTSC and further enrollment was approved.

Per 5F9003 Study Protocol Amendment 10, a separate DLBCL Phase 2 Cohort 4 was opened using modified inclusion criteria and an interim efficacy analysis will be performed for this cohort after 20 efficacy-evaluable patients are available to determine whether further enrollment in the cohort will continue up to 100 patients.

2.1.3. Unplanned Interim Analysis 1

An unplanned interim safety analysis 1 of available study data using a data cut date of 01 April 2021 was performed to support potential regulatory submission of the use of magrolimab in MDS.

2.1.4. Unplanned Interim Analysis 2

An unplanned interim safety analysis 2 of available study data using a data cut date of 17 March 2023 was performed to support potential regulatory submission of the use of magrolimab in MDS.

2.2. Final Analysis

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

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

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

By-patient listings will be presented for all patients in the All Enrolled Analysis Set and sorted by dose level assigned, patient ID number, visit date, and time (if applicable). Data collected on log forms, such as AEs, will be presented in chronological order by patient. The dose level to which patients were initially assigned will be used in the listings. Age, sex at birth, race, and ethnicity information will be included in the listings, as space permits.

3.1. Analysis Sets

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

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

3.1.1. Enrolled Analysis Set

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

3.1.2. Safety Analysis Set

The Safety Analysis Set (SAF) includes all patients who received at least 1 dose of any study treatment. This is the primary analysis set for safety, demographics, and medical/cancer history.

3.1.3. Efficacy Analysis Set

The Efficacy Analysis Set (EAS) includes all enrolled patients who received at least 1 dose of magrolimab.

3.1.4. Dose-Limiting Toxicity Analysis Set 1

The DLT Analysis Set 1 includes all enrolled Phase 1b patients in the magrolimab + rituximab cohort who met EITHER of the following criteria:

- The patient experienced a DLT
- The patient completed at least 3 infusions of magrolimab and 2 infusions of rituximab

3.1.5. Dose-Limiting Toxicity (DLT) Analysis Set 2

The DLT Analysis Set 2 includes all enrolled Phase 1b patients in the magrolimab + R-GemOx cohort who met EITHER of the following criteria:

- The patient experienced a DLT at any time after initiation of the first infusion of magrolimab, rituximab, and gemcitabine or oxaliplatin
- The patient completed at least 3 infusions of magrolimab and 2 infusions of rituximab, and 1 infusion of gemcitabine and oxaliplatin

3.2. Patient Grouping

Analyses will be presented by phase and treatment combination, with patients further grouped by cohort, unless otherwise specified, as follows:

- Phase 1b, Antibody Combination
  - Phase 1b Cohort 1 : Magro 10 mg/kg no load + Ritux
  - Phase 1b Cohort 2 : Magro 20 mg/kg no load + Ritux
  - Phase 1b Cohort 3 : Magro 30 mg/kg load + Ritux
  - Phase 1b Cohort 4 : Magro 45 mg/kg load + Ritux
- Phase 2, Antibody Combination
  - Phase 2 Cohort 1 : Magro 30 mg/kg no load + Ritux (RP2DS)
  - Phase 2 Cohort 2 : Magro 30 mg/kg load + Ritux
  - Phase 2 Cohort 3 : Magro 45 mg/kg load + Ritux
  - Phase 2 Cohort 4 : DLBCL Magro 30 mg/kg no load + Ritux
- Phase 1b, Chemotherapy Combination
  - Phase 1b Cohort 5 : Magro 30 mg/kg mix load + R-GemOx
  - Phase 1b Cohort 6: Magro 45 mg/kg load + R-GemOx

where Magro stands for magrolimab with dose level corresponding to the maintenance dose, load or no load corresponding to whether a loading dose of magrolimab was given, Ritux stands for Rituximab 375 mg/m^2 and R-GemOx stands for Rituximab 375 mg/m^2 + Gemcitabine 1000 mg/m^2 + Oxaliplatin 100 mg/m^2. The details of each dosing regimen for are described in Table 1 to Table 3.

Efficacy analyses will be presented by dose and disease type, and by disease, as follows:

- Phase 1b and 2, Antibody Combination
  - Magro 10 mg/kg + Ritux diffuse large B-cell lymphoma (DLBCL)
  - Magro 10 mg/kg + Ritux indolent lymphoma (IL)
  - Magro 10 mg/kg + Ritux DLBCL + IL
  - Magro 20 mg/kg + Ritux DLBCL
  - Magro 20 mg/kg + Ritux IL
  - Magro 20 mg/kg + Ritux DLBCL + IL
  - Magro 30 mg/kg + Ritux DLBCL
  - Magro 30 mg/kg + Ritux IL
  - Magro 30 mg/kg + Ritux DLBCL + IL
  - Magro 45 mg/kg + Ritux DLBCL
  - Magro 45 mg/kg + Ritux IL
  - Magro 45 mg/kg + Ritux DLBCL + IL
- Phase 1b, Chemotherapy Combination
  - Magro 30 mg/kg + Chemo DLBCL
  - Magro 45 mg/kg + Chemo DLBCL

Actual magrolimab maintenance dose levels (MDL) will be defined as the maximum non-priming dose during Cycle 1 and 2, categorized by:

- 10 mg/kg: if 8.5 mg/kg < MDL <= 15 mg/kg
- 20 mg/kg: if 15 mg/kg < MDL <= 25 mg/kg
- 30 mg/kg: if 25 mg/kg < MDL <= 35 mg/kg
- 45 mg/kg: if 35 mg/kg < MDL < 50 mg/kg

If a magrolimab infusion interruption due to AE occurred, the actual magrolimab maintenance dose level will default to the assigned dose upon enrollment. Priming doses will be defined as actual magrolimab doses below 2 mg/kg and priming doses beyond the first dose for a patient will be defined as a re-priming dose.

3.3. Strata and Covariates

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

3.4. Examination of Patient Subgroups

No patient subgroup analyses will be performed.

3.5. Multiple Comparisons

Adjustments for multiplicity will not be made because no formal statistical testing will be performed in this analysis.

3.6. Missing Data and Outliers

3.6.1. Missing Data

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

For missing last dosing date of study drug, imputation rules are described in Section 4.2.1. The handling of missing or incomplete dates for AE onset in Section 7.2.5.2, and for prior and concomitant medications in Section 7.5.

3.6.2. Outliers

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

3.7. Data Handling Conventions and Transformations

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

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

In general, age (in years) on the date of the first dose of study drug will be used for analyses and presented in listings. If age at Day 1 is not available for a patient, then age derived based on date of birth and the Day 1 visit date will be used instead. If an enrolled patient was not dosed with any study drug, the enrollment date will be used instead of the Day 1 visit date. For screen failures, the date the first informed consent was signed will be used for the age derivation. Age required for longitudinal and temporal calculations and analyses (eg, estimates of creatinine clearance, age at date of AE) will be based on age derived from date of birth and the date of the measurement or event, unless otherwise specified.

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

- A value that is 1 unit less than the LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "< x" (where x is considered the LOQ). For example, if the values are reported as < 50 and < 5.0, values of 49 and 4.9, respectively, will be used to calculate summary statistics. An exception to this rule is any value reported as < 1 or < 0.1, etc. For values reported as < 1 or < 0.1, a value of 0.9 or 0.09, respectively, will be used to calculate summary statistics.

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

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

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

3.8. Analysis Visit Windows

3.8.1. Definition of Study Day

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

3.8.2. Analysis Visit Windows

The nominal visit as recorded on the CRF will be used when data are summarized by visit. Any data relating to unscheduled visits will not be assigned to a particular visit or time point. However, the following exceptions will be made:

- An unscheduled visit prior to the first dosing of study drug may be included in the calculation of the baseline value, if applicable.

- Unscheduled visits after the first dosing of study drug will be included in determining the maximum postbaseline toxicity grade.

- Data collected on a follow-up visits will be summarized as a separate visits.

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

Depending on the statistical analysis method, single values may be required for each analysis window. For example, change from baseline by visit usually requires a single value, whereas a time-to-event analysis would not require 1 value per analysis window.

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

- For baseline, the last nonmissing value on or prior to first dosing date of study drug will be selected, unless specified differently. If there are multiple records with the same time or no time recorded on the same day, the baseline value will be the average of the measurements for continuous data, or the measurement with the lowest severity (eg, normal will be selected over abnormal for safety electrocardiogram [ECG] findings) for categorical data.

- For postbaseline values:

  — The record closest to the nominal day for that visit will be selected.

  — If there are 2 records that are equidistant from the nominal day, the later record will be selected.

  — If there is more than 1 record on the selected day, the average will be taken for continuous data and the worse severity will be taken for categorical data, unless otherwise specified.

4. PATIENT DISPOSITION

4.1. Patient Enrollment and Disposition

A summary of site patient enrollment will be provided by phase and treatment combination across cohorts. The summary will present the number and percentage of patients enrolled at each country and site. For each column, the denominator for the percentage calculation will be the total number of patients analyzed for that column.

A summary of treatment disposition will be provided by phase and treatment combination across cohorts. This summary will present the number of patients and percentage of patients in each of the categories listed below:

- Did not receive magrolimab
- Received magrolimab priming dose only
- Primary reason for discontinuation of magrolimab without any maintenance dose
- Received magrolimab maintenance dose
- Primary reason for discontinuation of magrolimab

The above summaries of did not receive magrolimab, and primary reason for discontinuation of magrolimab, would similarly be repeated for rituximab, gemcitibine, and for oxticibine, as applicable.

A summary of study disposition will be provided by phase and treatment combination across cohorts. This summary will present the number of patients in each of the categories listed below:

- Study status (on treatment, in follow-up, off study)
- Primary reason for study exit (withdrawal of consent for follow-up, lost to follow-up, study terminated by sponsor, death, other)
- Time on study treatment (months)
- Time on study (months)

For study status and primary reason for study exit, the number and percentage of patients in each category will be provided. For time on study treatment and study, descriptive statistics will be provided.

The denominator for the percentage calculation will be the total number of patients in the Enrolled Analysis Set corresponding to that column.

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

- Enrollment
- Patients who discontinued treatment
- Patients who discontinued from study

4.2. Extent of Study Drug Exposure

Extent of exposure to study drug will be examined by assessing the total duration of exposure to study drug specified in the protocol. This will be summarized by phase and treatment combination across cohorts for each study drug: magrolimab, rituximab, gemcitabine, and oxaliplatin, as applicable.

4.2.1. Duration of Exposure to Study Drug

Total duration of exposure to study drug will be defined as last dosing date of any study drug minus first dosing date plus 1, 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). If the last study drug dosing date is missing,

- If the study drug is permanently withdrawn, the latest date among the study drug end date, start date of AE leading to study treatment discontinuation, clinical visit date, laboratory sample collection date, and vital signs assessment date that occurred during the on-treatment period will be used for patients included in the final analyses or the last available date.
- If the study drug completion status is unknown, the earlier of the date of death or data snapshot date for analysis will be used.

The total treatment duration (in months), total number of infusions, and cumulative dose administratered (in grams) will be summarized using descriptive statistics. The number and percentage of patients with any re-priming dose (only applicable to magrolimab), missed or delayed doses, missed or delayed doses due to AE, dose reductions, and dose interruptions will be summarized. Dose interruptions will be further broken down by those due to AE and duration of interruptions due to AE (in minutes). Summaries will be provided by phase and treatment combination for each cohort for the Safety Analysis Set.

By-subject listings of study drug administration will be provided.

4.3. Protocol Deviations

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

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 (eg, nonadherence to study drug, violation of select inclusion/exclusion criteria) will be summarized by phase and treatment combination across cohorts for the Enrolled Analysis Set. A by-patient listing will be provided for those patients with important protocol deviation(s).

4.4. Assessment of COVID-19 Impact

This study was ongoing during the novel coronavirus disease 2019 (COVID-19) pandemic, and the COVID-19 pandemic has caused a disruption in the regular visit schedules for this study. Some patients were unable to attend onsite visits due to shelter in place guidelines, site closures, or other reasons. This section provides how to handle special situations due to COVID-19 in the analysis.

AEs due to COVID-19 will be included in AE analyses if applicable. A by-patient listing of Adverse Events due to COVID-19 will be provided.

4.4.1. Study Drug or Study Discontinuation Due to COVID-19

A by-patient listing of reasons for premature study drug or study discontinuation due to COVID-19 will be created.

4.4.2. Protocol Deviations Due to COVID-19

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

4.4.3. Missed and Virtual Visits due to COVID-19

A by-patient listing of patients with missed or virtual visits due to COVID-19 will be provided by patient ID number in ascending order.

Information regarding virtual or missed visits due to COVID-19 was collected as free text in the CRF comment fields. The determination of missing or virtual visits due to COVID-19 was done using Natural Language Processing (NLP) to search the CRF comment fields. A detailed explanation of the algorithm is given in Appendix 1.

5. BASELINE CHARACTERISTICS

5.1. Demographics and Baseline Characteristics

Patient demographic variables (ie, age, sex, race, and ethnicity) and baseline characteristics (body weight [in kg], height [in cm], body mass index [BMI; in kg/m^2], body surface area [in m^2]) will be summarized by phase and treatment combination for each cohort and overall using descriptive statistics for continuous variables and using number and percentage of patients for categorical variables.

Other baseline characteristics include:

- ECOG performance status (0, 1, 2, >2)
- DLBCL subcategories (transformed DLBCL, de novo DLBCL)
- Indolent lymphoma types (follicular lymphoma, marginal zone lymphoma)
- Lugano stage at initial diagnosis (I-II, III-IV, unknown)
- Cell of origin (activated B-cell, germinal center B-cell, unknown, not applicable)

Demographics and baseline characteristics will be summarized by phase and treatment combination for each cohort and overall using descriptive statistics for continuous variables and using number and percentage of patients for categorical variables. Summaries will be provided for the Enrolled Analysis Set.

By-patient demographics and baseline characteristics listings will be provided by patient ID number in ascending order.

5.2. Medical History

Medical history data were collected at screening and will be listed only.

5.3. Prior Anti-cancer Therapy

A by-subject listing of prior anti-cancner therapies will be provided by subject ID in ascending order.

6. EFFICACY ANALYSES

6.1. Primary Efficacy Endpoint

6.1.1. Definition of the primary Efficacy Endpoint

The primary efficacy endpoint of this study is the objective response rate (ORR) as defined by the investigator according to the Lugano Classification for lymphomas. The objective response rate is calculated as proportion of subjects who achieved either complete remission (CR) or partial remission (PR), which are based on disease assessment before any new anti-cancer therapy, if any. Subjects with no assessment available after start date of any study drug will be considered as non-responder.

6.1.2. Analysis Method of the Primary Efficacy Endpoint

The analyses will be based on the Efficacy Analysis Set. Summary tables with best response and objective response rate will be provided for the Efficacy Analysis Set. The point estimates for ORR and correspoindg 2-sided exact 95% CIs based on the Clopper-Pearson method will be provided.

6.2. Secondary Efficacy Endpoints

6.2.1. Definition of Secondary Efficacy Endpoints

Objective Response Rate (ORR): Objective response rate is defined as the proportion of patients who achieved CR+PR as determined by Lymphoma Response to Immunomodulatory therapy Criteria (LYRIC; {Cheson 2016}) while on study prior to the initiation of the subsequent line of anti-cancer therapy. According to Table 10-2 of the protocol, the criteria for CR and PR under LYRIC is the same as the criteria under Lugano. Response assessments on/after the initiation of the subsequent line of anti-cancer therapy will be excluded from deriavation.

Duration of Response (DOR): The DOR is measured from when the first (objective) response is met (i.e., CR or PR) until the first date of objectively documented progressive disease while on study prior to the initiation of the subsequent line of anti-cancer therapy. Patients who do not have objectively documented progressive disease will be censored at the last response assessment date. Response assessments after the initiation of the subsequent line of anti-cancer therapy will be excluded from deriavation.

Progression-free Survival (PFS): The PFS is measured from dose initiation until the first date of objectively documented progressive disease or death while on study prior to the initiation of the subsequent line of anti-cancer therapy. Patients who do not have progressive disease AND not died will be censored at the last response assessment date. Response assessments after the initiation of the subsequent line of anti-cancer therapy will be excluded from deriavation.

Overall Survival (OS): The OS is measured from dose initiation until death. Patients who did not die will be censored at their last known alive date.

Time to Progression (TTP): The TTP is measured from dose initiation until the first date of objectively documented progressive disease while on study prior to the initiation of the subsequent line of anti-cancer therapy. Patients who do not have objectively documented progressive disease will be censored at the last response assessment date. Response assessments after the initiation of the subsequent line of anti-cancer therapy will be excluded from deriavation.

6.2.2. Analysis Methods for Secondart Efficacy Endpoints

Objective Response Rate (ORR) : The point estimates for ORR and correspoindg 2-sided exact 95% CIs based on the Clopper-Pearson method will be provided.

Duration of Response (DOR): Duration of reponses will be base on patients with best response of complete or partial response. The median, first quartile (Q1) and third quartile (Q3) of DOR and time to objective response distribution will be estimated using the Kaplan-Meier method and the 95% CI on median will be provided.

Progression-free Survival: Medians, Q1, Q3 of the progression-free survival distributions, and the proportion of patients who are progression-free at 4, 6, 8, 12 and 15 months from the first dose of any study treatment will be estimated along with the 95% CI on median using the Kaplan-Meier method.

Overall Survival: Medians, Q1, Q3 of the overall survival distributions, and the proportion of patients with death at 4, 6, 8, 12, 15 and 24 months from the first dose of any study treatment will be estimated along with the 95% CI on median using the Kaplan-Meier method.

Time to Progression: Medians, Q1, Q3 of the time to progression, and the proportion of patients who with disease progression at 4, 6, 8, 12, 15 and 24 months from the first dose of any study treatment will be estimated along with the 95% CIs on median using the Kaplan-Meier method.

7. SAFETY ANALYSES

Safety analyses will be presented by phase and treatment combination, with patients further grouped by cohort, as specified in Section 3.2.

7.1. Primary Safety Endpoint in Phase 1b

7.1.1. Definition of the primary Safety Endpoint in Phase 1b

The primary safety endpoint in phase 1b of the study is dose-limiting toxicity evaluation (DLT) for DLT-evaluable patients.

DLT adverse events are determined by investigators by checking "Check if event is a DLT" in the Adverse Event CRF.

For patients in the magrolimab + rituximab cohort:

DLTs applied only to patients in the phase 1b part of the study for the magrolimab + rituximab cohort if either of the following criteria were met during the assessment period:

- The patient experienced a DLT.
- The patient completed at least 3 infusions of magrolimab and 2 infusions of rituximab.

For the Phase 1b part of the study, patients who withdrew before completing the 4-week DLT assessment period for reasons other than a DLT, or who do not fulfill either of the criteria above, were not evaluable for assessment of DLT for dose review decisions and were replaced in the cohort.

A DLT was defined as any Grade 3 or greater AE that is assessed as related to study drug (magrolimab and/or rituximab) that occurred during the 4-week DLT observation period.

The following events were exceptions to the DLT definition and were NOT considered a DLT:

- Grade 3 anemia, however, Grade 3 hemolytic anemia that is medically significant, requires hospitalization or prolongation of existing hospitalization, is disabling, or limits self-care activities of daily life (ADL) is considered a DLT.
- Grade 3 indirect/unconjugated hyperbilirubinemia that resolves to ≤ Grade 2 with supportive care within 1 week and is not associated with other clinically significant consequences.
- Isolated Grade 3 electrolyte abnormalities that resolve to ≤ Grade 2 with supportive care within 1 week and are not associated with other clinically significant consequences.

- Grade 3 elevation in alanine aminotransferase (ALT), aspartate aminotransferase (AST), or alkaline phosphatase that resolves to ≤ Grade 2 with supportive care within 1 week and is not associated with other clinically significant consequences.

- Transient Grade 3 nausea, vomiting, diarrhea, local reactions, influenza-like symptoms, myalgias, fever, headache, or acute pain that resolves to ≤ Grade 2 within ≤ 72 hours with supportive care.

- Grade 3 fatigue that resolves to ≤ Grade 2 within 2 weeks on study

- Grade 3 magrolimab or rituximab-related infusion reactions in the absence of an optimal pretreatment regimen, which is defined as acetaminophen or a comparable non-steroidal anti-inflammatory agent, plus an antihistamine and corticosteroids.

- Grade 3 tumor lysis syndrome or related electrolyte disturbances (hyperkalemia, hypophosphatemia, hyperuricemia) that resolve to ≤ Grade 2 within 7 days

- Grade 3 or 4 lymphopenia

- Grade 3 infusion reactions attributed to rituximab; an infusion reaction can only be attributed to rituximab alone if the infusion reaction occurs after the start of rituximab infusion, but prior to magrolimab infusion, on days where rituximab and magrolimab are both dosed

For patients in the magrolimab + R-GemOX cohort:

Patients enrolled in the safety dose-escalation part of the Phase 1b magrolimab + R-GemOx cohort are considered evaluable for assessment of DLT if EITHER of the following criteria are met during the DLT assessment period:

- The patient experienced a DLT at any time after initiation of the first infusion of magrolimab, rituximab, and gemcitabine or oxaliplatin.

- The patient completed at least 3 infusions of magrolimab, 2 infusions of rituximab, and 1 infusion of gemcitabine and oxaliplatin.

A DLT in this magrolimab + R-GemOx cohort is defined by the criteria for magrolimab + rituximab cohort listed above, with the additional definitions listed below:

- ≥ Grade 4 hematologic toxicity that does not resolve to ≤ Grade 2 and delays initiation of cycle 2 by more than 14 days.

- ≥ Grade 4 febrile neutropenia or associated infections

- ≥ Grade 4 non-hematologic toxicity that does not resolve or decrease to ≤ Grade 2 within 1 week.

- ≥ Grade 4 IRR

- Recurrent ≥ Grade 3 magrolimab, rituximab, gemcitabine, or oxaliplatin IRR despite optimal pretreatment regimen, which is defined as acetaminophen or a comparable non-steroid anti-inflammatory agent, plus an antihistamine and corticosteroids. In addition to the above, optimal pretreatment regimen includes antiemetic pretreatment for gemcitabine and/or oxaliplatin IRRs.

7.1.2. Analysis Method of the Primary Safety Endpoint in Phase 1b

The number and percentage of patients who experienced at least 1 DTLs will be provided and summarized by treatment cohort. A listing of DLT will also be provided.

7.2. Adverse Events and Deaths

7.2.1. Adverse Event Dictionary

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

7.2.2. Adverse Event Severity

Adverse events are graded by the investigator as Grade 1, 2, 3, 4, or 5 according to CTCAE Version 4.03. The severity grade of events for which the investigator did not record severity will be categorized as “missing” for tabular summaries and data listings. The missing category will be listed last in summary presentation.

7.2.3. Relationship of Adverse Events to Study Drug

Related AEs are those for which the investigator selected “Related” on the AE CRF to the question of “Relationship to magrolimab”, “Relationship to rituximab”, “Relationship to gemcitabine”, or “Relationship to oxaliplatin”. 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.

7.2.4. Serious Adverse Events

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

7.2.5. Treatment-Emergent Adverse Events

7.2.5.1. Definition of Treatment-Emergent Adverse Events

Treatment-emergent adverse events (TEAEs) are defined as 1 or both of the following:

- Any AEs with an onset date on or after the study drug start date and no later than 30 days after the last dose of any study drug or the initiation of the subsequent line of anti-cancer therapy, whichever is earlier
- Any AEs leading to discontinuation of study drug.

7.2.5.2. Incomplete Dates

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

- The AE onset is the same as or after the month and year (or year) of the first dosing date of study drug, and
- The AE onset date is the same as or before the month and year (or year) of the date corresponding to 30 days after the date of the last dose of study drug

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

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

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

7.2.6. Summaries of Adverse Events and Deaths

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

7.2.6.1. Summaries of TEAEs

A brief, high-level summary of AEs will be provided by treatment group and by the number and percentage of patients who experienced:

- Any TEAE
- Any Grade ≥ 3 TEAE
- Any Grade 5 TEAE
- Serious TEAE
- TEAE leading to discontinuation of any study treatment, by magrolimab, rituximab, gemcitabine, and oxaliplatin, as applicable, and any study drug
- Any TEAE of special interest
- Any TEAE of other important safety topics
- Any Grade ≥ 3 TEAE related to any study treatment
- Any Grade 5 TEAE related to any study treatment
- Any TEAE related to any study treatment leading to discontinuation of study by magrolimab, rituximab, gemcitabine, and oxaliplatin, as applicable, or any study drug

The high-level summary will be repeated analyzing AEs by dose level as follows:

- Phase 1b + 2, Antibody Combination
  - Magro 10 mg/kg + Ritux
  - Magro 20 mg/kg + Ritux
  - Magro 30 mg/kg + Ritux
  - Magro 45 mg/kg + Ritux
- Phase 1b, Chemotherapy Combination
  - Magro 30 mg/kg + R-GemOx
  - Magro 45 mg/kg + R-GemOx

The number and percentage of patients who experienced at least 1 TEAE will be provided and summarized by SOC, PT, and severity where applicable within each treatment combination for the AE categories below:

- TEAEs
- TEAEs related to magrolimab
- TEAEs leading to death
- Treatment-emergent SAEs
- Treatment-emergent SAEs related to magrolimab
- TEAEs leading to magrolimab discontinuation
- TEAEs leading to magrolimab infusion interruption
- TEAEs leading to magrolimab dose delay or dose reduction
- Grade 3 or higher TEAEs by SOC, PT, and severity

The number and percentage of patients who experienced at least 1 TEAE will be provided and summarized by PT and severity in descending order of total frequency:

- TEAEs by PT and severity

For the AE categories described below, summaries will be provided by PT in descending order of total frequency:

- TEAEs
- Grade 3 or higher TEAEs
- TEAEs leading to death
- Treatment-emergent SAEs

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

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

- All AEs, indicating whether the event is treatment emergent
- Treatment-emergent SAEs
- Adverse events leading to death

7.2.6.2. Summary of Deaths

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

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

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

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

A listing for deaths will also be provided.

7.2.7. Additional Analysis of Adverse Events

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

A brief, high-level summary of the number and percentage of patients who experienced at least 1 TEAEs of special interest will be provided by treatment cohort and category. A similar summary will be provided for other important safety topics.

- Any TEAE
- Any Grade ≥ 3 TEAE
- Any Grade 5 TEAE
- TEAEs related to any study treatment, and magrolimab
- Any Grade ≥ 3 TEAE related to any study treatment, and magrolimab
- Any Grade 5 TEAE related to any study treatment, and magrolimab
- TEAE leading to discontinuation of any study treatment, and magrolimab

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

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

7.2.7.2. Other Important Safety Topics

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

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

7.2.7.3. Regrouped AE Terms

For the regrouped AE preferred terms described below, a brief, high-level summary will be provided by treatment cohort:

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

7.3. Laboratory Evaluations

Laboratory data collected during the study will be analyzed and summarized using both quantitative and qualitative methods. Summaries of laboratory data will be provided for the Safety Analysis Set and will include data collected up to the last dose of study drug plus 30 days for patients who have permanently discontinued study drug or the initiation of the subsequent line of anticancer therapy, whichever is earlier, or all available data at the time of the database snapshot for patients who were ongoing at the time of an interim analysis. The analysis will be

based on values reported in conventional units. When values are below the LOQ, they will be listed as such, and the closest imputed value will be used for the purpose of calculating summary statistics as specified in Section 3.7.

7.3.1. Graded Laboratory Values

CTCAE Version 4.03 will be used to assign toxicity grades (0 to 4) to laboratory results for analysis. Grade 0 includes all values that do not meet the criteria for an abnormality of at least Grade 1. For laboratory tests with criteria for both increased and decreased levels, analyses for each direction (ie, increased, decreased) will be presented separately. Local labs will be graded based on the central lab normal ranges with in-house macro. In the event that both central and local lab results are collected in the clinical database, the worst toxicity grade will be used for the summary of lab toxicities.

7.3.1.1. Treatment-Emergent Laboratory Abnormalities

Treatment-emergent laboratory abnormalities are defined as values that increase at least 1 toxicity grade from baseline at any postbaseline time point, up to and including the date of last dose of study drug plus 30 days for patients who permanently discontinued study drug or the initiation of the subsequent line of anticancer therapy, whichever is earlier, or the last available date in the database snapshot for patients who were still on treatment at the time of the final analysis. If the relevant baseline laboratory value is missing, any abnormality of at least Grade 1 observed within the time frame specified above will be considered treatment emergent.

7.3.1.2. Summaries of Laboratory Abnormalities

All laboratory parameters for serum chemistry and hematology will be summarized. The number and percentage of patients for laboratory abnormalities will be provided by laboratory test and dose level within each phase and treatment combination for the worst treatment-emergent laboratory abnormalities postbaseline grade. Shift tables will also be provided to assess changes in severity grade from baseline to the worst treatment-emergent laboratory abnormalities postbaseline grade. The summaries will use the number of patients in the Safety Analysis Set as the denominator.

A listing of grade 3 or 4 treatment-emergent laboratory abnormalities for hematology and chemistry will be provided.

7.4. Body Weight and Vital Signs

No summary or listing of vital signs will be provided for synoptic CSR. Body weight is summarized in baseline characteristics in Section 5.1.

7.5. Pre, Prior, and Concomitant Medications

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

7.5.1. Pre Medications

Premedications are defined as any medications taken before a patient took the first two doses of magrolimab (including the priming dose), as record on the Pre-Medications eCRF form.

The optimal pretreatment regimen is defined as acetaminophen/paracetamol plus an antihistamine (i.e., oral acetaminophen 650 mg to 1000 mg (4 g/day maximum dose) and oral of IV diphenhydramine 25 to 50 mg or comparable regimen) plus IV dexamethasone 4 to 20 mg, or comparable regimen.

Premedication is required before administration of the first two doses of magrolimab.

- Premedication is also required for the repriming dose and the first maintenance dose.
- Premedication for subsequent magrolimab treatments may be continued based on the treating physician's clinical judgement and the presence/severity of prior infusion reactions where allowed

No summary of premedications will be provided. All the premidications will be provided in a by-subject listing sorted by subject ID number and start date in chronological order.

7.5.2. Prior Medications

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

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

No summary of prior medications will not be provided.

7.5.3. Concomitant Medications

Concomitant medications are defined as medications taken while a patient took study drug.

For the purposes of analysis, any medications with a start date prior to or on the first dosing date of study drug and continued to be taken after the first dosing date, or started after the first dosing date but prior to or on the last dosing date of study drug will be considered concomitant medications. Medications started and stopped on the same day as the first dosing date or the last dosing date of study drug will also be considered concomitant. Medications with a stop date prior to the date of first dosing date of study drug or a start date after the last dosing date of study drug will be excluded from concomitant medication. If a partial stop date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) prior to the date of first study drug administration will be excluded from the concomitant medication summary. If a partial start date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) after the study drug stop date will be excluded from the concomitant medication category.

No summary of concomitant medications will be provided. All prior and concomitant medications (other than per-protocol study drugs) will be provided in a by-patient listing sorted by patient ID number and administration date in chronological order. A listing of transfusions will also be provided.

7.6. Electrocardiogram Results

No rummary or listing of ECG assessment results will be provided.

7.7. Other Safety Measures

A by-subject listing of pregnancy test will be provided.

7.8. Changes From Protocol-Specified Safety Analyses

None.

8. PHARMACOKINETIC (PK) AND IMMUNOGENICITY ANALYSES

PK and immunogenicity analyses were performed separately and are not described in this SAP.

9. BIOMARKER ANALYSIS

CCI [redacted]. Additional details will be provided separately by the biomarker sciences group.

10. REFERENCES

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Mounier N, El Gnaoui T, Tilly H, Canioni D, Sebban C, Casasnovas RO, et al. Rituximab plus gemcitabine and oxaliplatin in patients with refractory/relapsed diffuse large B-cell lymphoma who are not candidates for high-dose therapy. A phase II Lymphoma Study Association trial. Haematologica 2013;98 (11):1726-31.

Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 2016;127 (20):2375-90.

11. SOFTWARE

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

12. APPENDIX

Appendix 1. Determining Missing and Virtual Visits Due To Covid-19

This appendix describes the clinical trial site collection of COVID-19 data pertaining to missed/virtual visits and the data processing algorithm used to determine which visits were missing and which visits were virtual.

Data collection

A COVID-19 supplement to the eCRF Completion Guidelines (CCG) was provided by data management to instruct clinical trial sites with respect to data entry expectations pertaining to scenarios related to the COVID-19 pandemic. If a visit was missed, sites should enter "Visit missed due to COVID-19." If an in-person visit was conducted virtually, sites should enter "Virtual visit due to COVID-19."

Determination of Missed and Virtual visits

Natural Language Processing (NLP) was used to search the CRF comment fields to identify instances of "COVID-19" (or synonyms, see Appendix Table 1) and "Virtual" (or synonyms, see Appendix Table 1). The search terms are maintained in a global lookup table and can be modified to tune the NLP model. For any comments with COVID-19 search terms, assign "Missed visit" or "Virtual visit as follows:

1) If COVID-19 terms are identified through NLP and the visit date is missing, then result is "Missed Visit"
2) If COVID-19 and Virtual terms are identified through NLP for a visit, then result is "Virtual Visit". When there are multiple records for the same subject and the same visit, NLP will be based on multiple records to ensure 1 unique category per subject per visit
3) Otherwise result is missing

Appendix Table 1. Examples of search terms for "COVID-19" and "Virtual" used to identify missed and virtual visits.

Search terms for "COVID-19"	Search terms for "Virtual"
COVID19	VIRTUAL
CORONA	TELEMED
CORONAVIRUS	TELEHEALTH
PANDEMIC	TELEPHONE
OUTBREAK	REMOTE
CRISIS	TELEMEDICINE
LOCKDOWN	TELECONSULTATION
QUARANTINE	TELEPHONICALLY
SHELTER	PHONE
	HOME VISIT
	ZOOM
	SKYPE

5F9003-Final-SAP-v1.0

ELECTRONIC SIGNATURES

Signed by	Meaning of Signature	Server Date (dd-MMM-yyyy hh:mm:ss)
PPD	Clinical Development eSigned	20-May-2024 21:16:23
PPD	Biostatistics eSigned	20-May-2024 22:51:13