STATISTICAL ANALYSIS PLAN

Study Protocol Number:	AdvanTIG-101
Study Protocol Title:	A Phase 1b/2 Study Investigating the Safety, Tolerability, Pharmacokinetics, and Preliminary Antitumor Activity of Ociperlimab (BGB-A1217) in Combination With Tislelizumab (BGB-A317) or Rituximab in Patients With Relapsed or Refractory Diffuse Large B-Cell Lymphoma
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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
ADA	antidrug antibody
AE	adverse event
BGB-A1217	Ociperlimab
BGB-A317	Tislelizumab
BMI	Body Mass Index
CR	complete response
DLBCL	diffuse large B-cell lymphoma
DLT	dose-limiting toxicity
DOR	duration of response
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic case report form
EBV	Epstein-Barr virus
IHC	immunohistochemistry
imAE	immune-mediated adverse event
MedDRA	Medical Dictionary for Regulatory Activities
MTD	maximum tolerated dose
NCI-CTCAE	National Cancer Institute-Common Terminology Criteria for Adverse Events
ORR	overall response rate
OS	overall survival
PD	progressive disease
PD-L1	programmed cell death ligand-1
PET	positron-emission tomography
PFS	progression-free survival
PK	pharmacokinetic(s)
PR	partial response
R/R	relapsed or refractory
RP2D	recommended Phase 2 dose
SAE	serious adverse event
SAP	statistical analysis plan
SMC	Safety Monitoring Committee
TEAE	treatment-emergent adverse event

Abbreviation	Definition
TE	Treatment emergent
WHO DD	World Health Organization Drug Dictionary

1. INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to describe the procedures and the statistical methods that will be used to analyze and report results for AdvanTIG-101: A Phase 1b/2 Study Investigating the Safety, Tolerability, Pharmacokinetics, and Preliminary Antitumor Activity of Ociperlimab (BGB-A1217) in Combination With Tislelizumab (BGB-A317) or Rituximab in Patients With Relapsed or Refractory Diffuse Large B-Cell Lymphoma. The focus of this SAP is for the planned interim analysis for cohort 1 and the final analysis specified in the study protocol. This SAP is based on the protocol amendment 3.0 dated on 22 May 2024 and the electronic case report form.

2. STUDY OVERVIEW

This is a Phase 1b/2, open label, dose confirmation, and dose expansion study to evaluate the safety, tolerability, PK, and preliminary antitumor activity of ociperlimab in combination with tislelizumab or rituximab in patients with R/R DLBCL.

Each cohort will firstly conduct Dose Confirmation Stage to confirm the recommended phase II dose (RP2D) of ociperlimab. Then, the confirmed RP2D will be implemented in Dose Expansion Stage. Eligible patients will be allocated to 2 cohorts.

- Cohort 1: R/R DLBCL patients with positive PD-L1 on the surface of tumor cells will receive ociperlimab in combination with tislelizumab
- Cohort 2: Patients will receive ociperlimab in combination with rituximab
  - Dose Confirmation Stage: R/R DLBCL patients with negative PD-L1 on the surface of tumor cells.
  - Dose Expansion Stage: R/R DLBCL patients regardless of PD-L1 expression.

Approximately 43 to 50 patients in Cohort 1 and approximately 23 to 30 patients in Cohort 2 will be enrolled in the entire study. Every treatment cycle contains 21 days. The combination of ociperlimab with tislelizumab in Cohort 1 and ociperlimab with rituximab in Cohort 2 will be administrated intravenously on Day 1 of each 21-day cycle continuously until confirmed progressive disease (PD), death, withdrawal of consent, loss of follow-up, or study termination by sponsor, whichever occurs first.

Dose confirmation Stage:

Based on prior data of ociperlimab in combination with tislelizumab in solid tumors and a RP2D deemed at 900 mg ociperlimab combined with 200 mg tislelizumab (per Phase I study BGB-900-105), 2 dose levels (900 mg and 600 mg) of ociperlimab are selected for the combo as potential candidates for dose confirmation stage of this study.

Ociperlimab will be tested at the dose level of 900 mg initially. If ociperlimab 900 mg exceeds the MTD (i.e., with ≥ 1/3 of the DLT-evaluable patients on this dose level that experience DLT), ociperlimab 600 mg will then be tested. Other dose levels of ociperlimab (e.g., lower than 600 mg) may be explored to confirm the optimal dose level of ociperlimab in combination with

tislelizumab or rituximab per the SMC's recommendation considering the totality of emerging data. The dose of tislelizumab or rituximab will be fixed at 200 mg or 375 mg/m^2, respectively. Patients in both Cohort 1 and Cohort 2 will be monitored for DLTs for the first cycle (21 days after the first administration of the combination regimens).

RP2D confirmation will occur in accordance with the modified 3 + 3 principles as follows:

Three to 6 patients will be initially enrolled per dose level.

- If none of the initial 3 patients enrolled at a given dose level experiences a DLT (0/3), this dose level of ociperlimab in combination of tislelizumab or rituximab will be confirmed as RP2D.
- If 1 of the initial 3 patients enrolled at a given dose level experiences a DLT (1/3), at least 3 additional patients will be enrolled at this dose level (for a total of at least 6 evaluable patients).
  - If less than one-third of patients enrolled at a given dose level experiences a DLT (eg, < 2/6), this dose level of ociperlimab in combination of tislelizumab or rituximab will be confirmed as RP2D.
  - If ≥ 2 of the initial 6 patients enrolled at a given dose level experience a DLT, the MTD will be considered as having been exceeded and a next lower dose level will be assessed for toxicity in the same manner as described above. If ≥ 2 of the initial 6 patients enrolled at dose level of ociperlimab 600 mg experience DLT, other dose levels of ociperlimab (eg. lower than 600 mg) may be explored per the SMC's recommendation considering the totality of emerging data.

All available safety data, including AEs, laboratory assessments, PK, and preliminary efficacy analyses (as available), will be reviewed by the medical monitor and study team members from Pharmacovigilance/Drug Safety, Clinical Pharmacology, and Biostatistics with input from other members as appropriate.

RP2D will be confirmed after discussion with SMC before the initiation of dose expansion.

Dose expansion Stage:

After the RP2D of ociperlimab in combination with tislelizumab or rituximab are confirmed, further enrollment of both cohorts will commerce to their target sample size.

- Cohort 1: Approximately 40 patients will be enrolled at RP2D dose level. One futility interim analysis will be conducted when approximately 20 patients have been enrolled and meet the efficacy-analysis set definition. The SMC along with the sponsor will make the decision of proceeding or not. To reflect the natural distribution across PD-L1 expression given a relatively small sample size at interim analysis, the number of eligible patients with PD-L1 expression ≤ 5% on the surface of tumor cells as determined by local laboratory will be capped to ≤ 50% of the first 20 patients enrolled, and the benefit-risk profile may also be evaluated by the SMC and sponsor for these patients. After the interim analysis, the number of these patients with PD-L1 expression ≤ 5% on the surface

of tumor cells as determined by local laboratory may be further capped per the SMC's recommendation considering the totality of emerging data.

- Cohort 2: Approximately 20 patients will be enrolled at RP2D dose level.

All AEs will be graded according to the National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 5.0. Additional and specific information regarding AE monitoring and reporting is specified in protocol Section 9. Preliminary antitumor activity will be evaluated by the investigator using the Lugano Classification (Cheson et al 2014).

Samples for PK and ADA assessment will be collected for ociperlimab and tislelizumab (see protocol Section 8.6).

The study consists of four periods, including screening period, treatment period, safety follow-up period, and long term follow-up. Study procedures and assessments are further detailed in protocol Section 7 and Section 8, respectively, and the Schedule of Assessments can be found in protocol Appendix 1.

3. STUDY OBJECTIVES

3.1. Primary Objective

- To assess the safety and tolerability of ociperlimab (also known as BGB-A1217) in combination with tislelizumab (also known as BGB-A317) or rituximab in patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL)
- To confirm the recommended Phase 2 dose (RP2D) of ociperlimab when administered in combination with tislelizumab or rituximab in patients with R/R DLBCL

3.2. Secondary Objective

- To assess the preliminary antitumor activity of ociperlimab in combination with tislelizumab or rituximab in patients with R/R DLBCL as measured by investigator-assessed response using the Lugano Classification (2014)
- To characterize the pharmacokinetics (PK) of ociperlimab in combination with tislelizumab or rituximab
- To assess the host immunogenicity to ociperlimab in combination with tislelizumab or rituximab

3.3. Exploratory Objective

- To explore the correlation of programmed cell death ligand-1 (PD-L1) expression level and the preliminary antitumor activity of ociperlimab in combination with tislelizumab
- To characterize the exploratory biomarkers and their association with preliminary antitumor activity of ociperlimab in combination with tislelizumab or rituximab

4. STUDY ENDPOINTS

4.1. Primary Endpoint(s)

- Adverse events (AEs) and serious adverse events (SAEs) as characterized by type, frequency, severity (as graded by NCI-CTCAE Version 5.0), seriousness, and relationship to study drug(s); physical examinations, electrocardiograms (ECGs), laboratory abnormalities, and changes in laboratory assessments as needed; and AEs meeting protocol-defined dose-limiting toxicity (DLT) criteria
- RP2D of ociperlimab when administered in combination with tislelizumab or rituximab

4.2. Secondary Endpoints

- To evaluate the preliminary antitumor activity of ociperlimab in combination with tislelizumab or rituximab in patients with R/R DLBCL as measured by investigator-assessed response using the Lugano Classification (Cheson et al 2014) as measured by:
  - Overall response rate (ORR)
  - Complete response (CR) rate
  - Duration of response (DOR)
  - Time to response (TTR)
  - Progression-free survival (PFS)
  - Overall survival (OS)
- Serum concentration and PK parameters (as appropriate) of ociperlimab in combination with tislelizumab or rituximab
- Immunogenic responses to ociperlimab in combination with tislelizumab or rituximab, which will be evaluated through the detection of antidrug antibodies (ADAs)

4.3. Exploratory Endpoints

- Evaluate PD-L1 expression in archival or fresh patient-derived tumor tissue samples at screening and its association with the preliminary antitumor activity of ociperlimab in combination with tislelizumab
- Evaluate biomarkers from patient-derived tumor tissue and/or blood (or blood derivative) samples obtained before, during, and/or after treatment, and their association with preliminary antitumor activity of ociperlimab in combination with tislelizumab or rituximab. Biomarkers may include expression of T cell immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain (TIGIT), CD226, CD155, and CD112, PD-L1/2 gene alteration, Epstein-Barr virus (EBV) status, tumor microenvironment, immune-related gene expression profile, and gene mutation profile in tumor tissue; immune-cell quantification and phenotypes, cytokine profiling, immune-related gene expression profiling, and DNA/ circulating tumor DNA (ctDNA) sequencing in peripheral blood

5. SAMPLE SIZE CONSIDERATIONS

The study plans to enroll approximately 66 to 80 patients:

- Cohort 1: Approximately 43 to 50 patients
- Cohort 2: Approximately 23 to 30 patients

For Cohort 1, the sample size of approximately 40 patients at RP2D is based on the precision of the estimate of ORR, a consideration that a relatively sufficient number of patients is needed to justify performing further analysis (e.g., the subgroup analysis based on cutoff value of tumor PD-L1 expression), and a probability that is high enough to observe certain AEs of interest (e.g., rash). With 40 patients, if the observed ORR is 60%, the corresponding Clopper Pearson 95% CI will be 43.3% to 75.1%. For an AE with a rate of 10%, there is 98.5% probability to observe ≥ 1 event of such an AE among all 40 patients (multiple same AE on one patient will be counted only once). Considering the patients in the dose-confirmation stage that are not dosed at RP2D dose level (approximately 3 to 10 patients), approximately 43 to 50 patients in total will be enrolled in Cohort 1.

For Cohort 2, the sample size of approximately 20 patients at RP2D is based on the precision of the estimate of ORR. With 20 patients, if the observed ORR is 60%, the corresponding Clopper-Pearson 95% CI will be 36.1% to 80.9%. Considering the patients in the dose-confirmation stage that are not dosed at RP2D dose level (approximately 3 to 10 patients), approximately 23 to 30 patients in total will be enrolled in Cohort 2.

6. STATISTICAL METHODS

6.1. Analysis Sets

The Safety analysis set includes all patients who received any dose of any study drug(s). The Safety analysis set will be used for all safety analyses.

The Efficacy analysis set includes all patients who received any dose of any study drug(s), had evaluable disease at baseline, and had ≥ 1 evaluable postbaseline tumor response assessment unless any clinical PD or death occurred before the first postbaseline tumor assessment. The Efficacy analysis set will be used for all efficacy analyses.

The DLT-evaluable analysis set includes patients who 1) experienced a DLT event or 2) received ≥ 80% each scheduled study drug administration and remained on study during the DLT assessment window in the dose confirmation stage of each cohort. The DLT-evaluable analysis set will be used for all DLT-related summary analyses.

The PK analysis set includes all patients who received any dose of study drug(s), for whom any quantifiable postdose PK concentrations are available. The PK analysis set will be used for PK analyses.

The Immunogenicity analysis set includes all patients who received any dose of any study drug(s), for whom both baseline ADA and ≥ 1 postbaseline ADA results are available. The Immunogenicity analysis set will be used for immunogenicity analyses.

6.2. Multiplicity Adjustment

Not applicable.

6.3. Data Analysis General Considerations

6.3.1. Definitions and Computations

Study drugs include ociperlimab (900 mg or 600 mg, and potentially lower dose levels) in combination with tislelizumab (200 mg) or rituximab (375 mg/m^2).

Study day will be calculated in reference to the date of the first dose of study drugs. There is no study day 0. In the situation where the event date is partial or missing, the date will appear partial or missing in the listings. Study day and any corresponding durations will be presented based on the imputations specified in Appendix 1.

Unless otherwise specified, a baseline value is defined as the last non-missing value collected before the first dose of study drug.

All calculations and analyses will be conducted using SAS® Version 9.4 or higher.

6.3.2. Conventions

Unless otherwise specified, the following conventions will be applied to all analyses:

- 1 year = 365.25 days. Number of years is calculated as (days/365.25) rounded up to 1 significant digit.
- 1 month = 30.4375 days. Number of months is calculated as (days/30.4375) rounded up to 1 significant digit.
- Duration of image-based event endpoints (such as PFS) will be based on the actual date the radiograph was obtained rather than the associated visit date.
- For laboratory results collected as < or > a numeric value, 0.0000000001 will be subtracted or added, respectively, to the value.
- For by-visit observed data analyses, percentages will be calculated based on the number of patients with non-missing data as the denominator, unless otherwise specified.
- For continuous endpoints, summary statistics will include n, mean, standard deviation, median, Q1, Q3 and range (minimum and maximum).
- For discrete endpoints, summary statistics will include frequencies and percentages.

6.3.3. Handling of Missing Data

Missing data will not be imputed unless otherwise specified elsewhere in this SAP. Missing dates or partially missing dates will be imputed conservatively for adverse events and prior/concomitant medications/procedures. Specific rules for the handling of missing or partially missing dates for adverse events and prior/concomitant medications/procedures are provided in Appendix 1.

By-visit endpoints will be analyzed using observed data unless otherwise specified. For observed data analyses, missing data will not be imputed, and only the observed records will be included.

6.4. Patient Characteristics

6.4.1. Patient Disposition

The number (percentage) of patients treated, discontinued from the study, reasons for discontinued from the study, and the duration of study follow-up will be summarized in the safety analysis set. The patients who discontinued treatment and the primary reason for the end of treatment will be summarized among patients who were treated.

6.4.2. Protocol Deviations

Important protocol deviation criteria will be established, and patients with important protocol deviations will be identified and documented. Important protocol deviations will be summarized for all patients in the safety analysis set. They will also be listed by each category. Deviation categories are not mutually exclusive. Multiple deviations within the same category are counted once per patient.

6.4.3. Demographic and Other Baseline Characteristics

Demographics and other baseline characteristics will be summarized using descriptive statistics in the safety analysis set, including but not limited to the following variables:

- Age (continuously and by categories ≤75 or >75 years)
- Sex
- Race
- Ethnicity
- Weight
- BMI
- ECOG
- Hepatitis B Core Antibody
- Hepatitis C antibody

A listing of demographic and other baseline characteristics will be provided.

6.4.4. Disease History

The number (percentage) of patients reporting a history of disease and characteristics, as recorded on the eCRF, will be summarized in the Safety analysis set. Disease characteristics include but not limited to:

- Time since first diagnosis of DLBCL to first dose (months)
- Disease status (relapsed or refractory)

- DLBCL IHC subtype
- DLBCL GEP subtype
- Stage at study entry
- PD-L1 expression on tumor cell
- PD-L1 expression on immune cell
- Number (%) of patients with bulky disease
- Number (%) of patients with B-symptom
- Number (%) of patients with baseline bone marrow involvement
- Number (%) of patients with extra nodal sites
- Number (%) of patients with prior radiotherapy

A listing of disease history will be provided.

6.4.5. Prior Systemic Anticancer Therapies

Prior systemic anti-cancer therapies will be summarized in the safety analysis set. The variables include:

- Number (%) of patients with prior systematic therapy for DLBCL
- Number of lines of prior therapies and number of lines of prior therapies categorized as 1, 2, 3, etc.
- Time from the end of last therapy to first dose date (months)
- Time from end of last disease progression to first dose date (months)
- Reason last therapy ended
- Best overall response to last therapy

A listing of prior systemic anticancer drug therapies will be provided.

6.4.6. Prior and Concomitant Medications

Prior medication will be defined as the medication that started before the day of the first dose of study drugs. Concomitant medications will be defined as medications that (1) started before the first dose of study drugs and were continuing at the time of the first dose of study drugs, or (2) started on or after the date of the first dose of study drugs up to 30 days after the patient's last dose or the initiation of a new anti-cancer therapy.

Prior and concomitant medications will be coded using the version of World Health Organization Drug Dictionary (WHO DD) drug codes at the time of database lock. They will be further classified to the appropriate Anatomical Therapeutic Chemical (ATC) code.

The number (percentage) of patients reporting prior and concomitant medications will be summarized by ATC medication class and WHO DD preferred name in the Safety analysis set.

A listing of prior and concomitant medications will be provided.

6.4.7. Medical History

Medical History will be coded using Medical Dictionary for Regulatory Activities (MedDRA) Version at the time of database lock. The number (percentage) of patients reporting a history of any medical condition, as recorded on the CRF, will be summarized by system organ class and preferred term in the safety analysis set.

A listing of medical history will be provided.

6.5. Efficacy Analysis

Efficacy analyses will be conducted based upon investigators' tumor assessments using the Lugano Classification (2014) (Cheson et al 2014) in the efficacy analysis set, performed by cohort and dose level and by total.

ORR

ORR is defined as the proportion of patients achieving a best overall response of CR or PR. The point estimate and corresponding two-sided Clopper Pearson 95% CI for ORR will be presented.

The best overall response is defined as the best response recorded from the date of first dose of study drug(s) to the date of documented PD or new anticancer therapy, whichever occurs first. The proportion for each response category (e.g., CR, PR, stable disease [SD], and PD) will be presented.

For patients in the efficacy analysis set but with clinical PD or death occurring before the first postbaseline tumor assessment, their best overall response will be considered as PD or Not Assessable, respectively.

Rules for deriving ORR are presented in Table 1.

Table 1: Derivation rules for ORR

	Derivation rules
New anticancer therapy started prior to achieving a CR or PR	Patients starting any new anticancer therapy without achieving a CR or PR before will be considered as non-responders
Discontinuation of treatment not due to PD	Response assessment after discontinuation of treatment will be counted and used for analysis
No post-baseline response assessment (regardless of the reason)	Non-responders

CR rate

CR rate will be summarized with the same method as ORR.

PFS

PFS is defined as the time (months) from the date of first dose of study drug(s) to PD, as determined by the investigator, or death of any cause, whichever occurs first.

The distribution of PFS, including median, Q1 and Q3, and event-free rates at selected landmark timepoints such as 6 and 12 months, will be estimated using the Kaplan-Meier method. Two-sided 95% CIs of median and other quartiles will be constructed using the method of Brookmeyer and Crowley (Brookmeyer and Crowley 1982). 95% CIs for event-free rates will be calculated based on the Greenwood's formula (Greenwood 1926).

The censoring rules for PFS will follow the United States Food and Drug Administration Guidance for Industry Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics (US Food and Drug Administration 2018) and are presented in Table 2.

Table 2: Censoring rules for PFS

	Derivation rules	**Outcome**
No progression at the time of data cut-off or withdrawal from study or lost to follow up	Date of last adequate radiologic assessment prior to or on date of data cut-off or withdrawal from study	Censored
Discontinuation of the treatment not due to PD	Tumor assessment data collected after discontinuation of study treatment will be used for analysis	No impact
New anticancer therapy started prior to disease progression or death	Last adequate disease assessment before the new anticancer therapy	Censored
No baseline or post-baseline tumor assessments without death after first dose	Date of first dose	Censored
Death or progression after more than one missed visit	Date of last adequate radiologic assessment before missed tumor assessments	Censored

DOR

DOR for responders (CR or PR) is defined as the time (months) from the date of the earliest qualifying response (PR or better) to the date of PD, as determined by the investigator, or death for any cause, whichever occurs earlier.

The DOR censoring rule is following the rules for PFS as in Table 2. Kaplan-Meier methodology will be used to estimate the median and other quartiles and landmark event-free rates for DOR and with corresponding 95% CI provided. Only responders will be included in this analysis.

TTR

TTR for responders (CR or PR) is defined as the time (months) from the date of first dose of study drug(s) to the date of the earliest qualifying response (PR or better) as determined by the

investigator. TTR will be summarized by sample statistics, such as mean, median, and standard deviation for responders only.

OS

OS is defined as the time (months) from the date of first dose of study drug(s) to death due to any cause. OS will be analyzed using the similar method as described for PFS.

The censoring rules for OS are presented in Table 3.

Table 3: Censoring rules for OS

	Derivation rules	Outcome
Discontinuation of the treatment	Survival-related data collected after discontinuation of study treatment will be used for analysis	No impact
Patients' withdrawal from the study or lost to follow-up	Last known alive date prior to withdrawal or lost to follow-up	Censored
Missing visits	Ignored	No impact

Subgroup Analyses

Selected endpoints (e.g., ORR) will be summarized descriptively in PD-L1 subgroups (e.g., high vs. low in Cohort 1) and other subgroups based on baseline demographics (e.g., sex, age group) if deemed necessary and appropriate (i.e., when there is sufficient number of patients in the subgroup). Within-group summary statistics will be presented in forest plots. The subgroup variables and the cutoff values are subject to change if warranted to better represent the data.

If the cohort-wise total number of responders is observed to be low, detailed subgroup analysis could be waived.

6.6. Safety Analyses

All safety analyses will be performed by cohort and dose level and by total based on the safety analysis set. DLT related analyses will be based on the DLT evaluable set. Safety and tolerability will be assessed, where applicable, by incidence, severity, and change from baseline values for all relevant parameters including AEs, laboratory values, vital signs, ECG findings and physical examination.

6.6.1. Extent of Exposure

The following measures of the extent of exposure will be summarized by study drug:

- Duration of exposure (in weeks) will be calculated as (last date of exposure – first dose date + 1)/7, where the last date of exposure is the earliest date of (latest dose date + 20, end of study date, and data cutoff date).
- Number of treatment cycles received: defined as the total number of treatment cycles in which at least one dose of the study drug is administered.

- Total dose received per patient (in mg): defined as the cumulative dose of the study drug during the treatment period of the study.
- Actual dose intensity (in mg/three weeks): defined as the 21×total dose received (in mg) by a patient divided by (last dose date up to cutoff date +21 - first dose date).
- Relative dose intensity (%): defined as the ratio of the actual dose intensity and the planned dose intensity. Planned dose intensity (mg/cycle) is defined as the planned one cycle dose (mg).
- Number (%) of patients with dose delay
- Number (%) of patients with dose interruption
- Reasons for dose delay
- Reasons for dose interruption

6.6.2. Adverse Events

AEs will be graded by the investigators using CTCAE version 5.0. The AE verbatim descriptions (investigator terms from the eCRF) will be classified into standardized medical terminology using MedDRA. Adverse events will be coded to the MedDRA (Version for the study at the time of database lock) lowest level term closest to the verbatim term, along with the linked MedDRA preferred term (PT) and primary system organ class (SOC).

A treatment-emergent adverse event (TEAE) is defined as an AE that had onset date or increase in severity level from baseline on or after the date of the first dose of study drug through 30 days after the last dose (permanent discontinuation of study drug) or the initiation of new anti-cancer therapy, whichever is earlier. Worsening of any TEAE to Grade 5 beyond 30 days after the last dose of study drugs is also considered a TEAE (if it is prior to the initiation of new anticancer therapy). The TEAE classification also applies to imAEs that are recorded up to 90 days from the last dose of tislelizumab and/or ociperlimab, regardless of whether or not the patient starts a new antitumor therapy.

Summary tables will focus on those AEs that are treatment-emergent (TE). All AEs, treatment-emergent or otherwise, will be presented in patient data listings.

DLT events will be summarized for the dose confirmation phase.

An AE overview table, including the number and percentage of patients with any TEAEs, treatment-emergent serious adverse events (SAEs), TEAEs with Grade 3 or above, TEAEs that led to death, TEAEs that led to treatment discontinuation, TEAEs that led to dose delay, TEAEs that led to dose interruption, and treatment-related TEAEs will be provided. Treatment-related AEs include those events considered by the investigator to be related to study drug or with a missing assessment of the causal relationship.

The incidence of TEAEs will be also reported as the number (percentage) of patients with TEAEs by SOC, PT and the worst grade, by SOC and PT, and by PT in descending order. A patient will be counted only once by the highest severity grade within an SOC and PT, even if the patient experienced more than 1 TEAE within a specific SOC and PT.

Patient data listings of all AEs, AE leading to treatment discontinuation, AE leading to dose modification, AE leading to death, immune-mediated AE, and DLT will be provided.

All deaths and causes of death will be summarized, including those occurred during the study treatment period and those reported during the survival follow-up period after treatment completion/discontinuation. A listing of deaths will be provided.

6.6.3. Laboratory Values

A data listing of patients with grade 3 or higher postbaseline toxicity for selected lab parameters will be provided.

Other analysis such as descriptive summary statistics or changes from baseline by visit for laboratory parameters might be summarized if deemed necessary.

6.6.4. Vital Signs

Descriptive statistics for vital sign parameters systolic and diastolic blood pressure, pulse rate, temperature, and weight and change from baseline might be presented if deemed necessary.

6.6.5. Electrocardiograms (ECG)

Actual value and change from baseline for the ECG parameters (such as QT interval, heart rate, QTcF interval) might be presented by visit if deemed necessary.

6.6.6. Eastern Cooperative Oncology Group (ECOG) Performance Status

A shift table from baseline to worst post-baseline in ECOG performance status might be summarized if deemed necessary.

6.7. Pharmacokinetic Analyses

Serum concentration data and PK parameters (as appropriate) of ociperlimab and tislelizumab for each sampling time will be tabulated and summarized by visit/cycle for each treatment based on the PK analysis set. Descriptive statistics will include means, medians, ranges, and standard deviations, geometric means, and geometric CV%, as appropriate.

Additional PK analyses such as population PK analyses may be conducted as appropriate, and the results of such analyses may be reported separately from the clinical study report.

6.8. Immunogenicity Analyses

Anti-drug antibodies (ADAs) samples will be collected in this study as outlined in Protocol. The scope of ADAs calculations used for characterizing clinical immunogenicity depends on the incidence and kinetics of detected ADA. Therefore, not all parameters described below will be derived or additional parameters may be added. The effect of immunogenicity on PK, efficacy, and safety may be evaluated if data allows and will be reported separately from the CSR.

The immunogenicity results will be summarized using descriptive statistics by the number and percentage of subjects who develop detectable ADAs for ociperlimab and tislelizumab separately

based on Immunogenicity Analysis set. The incidence of positive and neutralizing ADAs (as applicable) will be reported for ADA-evaluable subjects according to the following definitions:

- **ADA-evaluable subject:** Number of subjects with reportable non-missing baseline result and at least one reportable sample taken after drug administration during the treatment or follow-up observation period with reportable result (used for computing treatment induced ADA incidence).
- **Treatment-emergent ADA:** The sum of both treatment-boosted and treatment-induced ADA-positive subjects as a proportion of the evaluable subject population. Synonymous with "ADA Incidence".
- **Treatment-induced ADA:** ADA-evaluable subjects that were ADA-negative at baseline and ADA-positive following administration of biologic product.
- Treatment-boosted ADA: Baseline-positive ADA-evaluable subjects with significant increases (4-fold or higher) in ADA titer after biologic drug administration. Baseline positive ADA-evaluable subject is an ADA-evaluable subject with positive ADA result at baseline.
- **Persistent ADA:** 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 samples (irrespective of any negative samples in between) are separated by a period of 16 weeks or longer, or treatment induced ADA incidence only in the last sampling time point of the treatment study period or at a sampling time point with less than 16 weeks before an ADA-negative last sample.
- **Transient ADA:** Treatment-induced ADA that is not considered as persistent ADA.
- **Neutralizing ADA:** patients with positive NAb.

The individual immunogenicity results will also be listed.

6.9. Other Analyses

Exploratory biomarker analyses will be performed in an effort to understand the association of markers of interest with study drug(s) response, such as efficacy.

7. INTERIM ANALYSES

One futility interim analysis for ORR is planned to be conducted when approximately 20 patients have been enrolled at RP2D dose level and meet the definition of efficacy analysis set with a non-binding futility boundary of 35% (equivalent to observe ≤ 7 responders) for Cohort 1. If the true ORR is as low as 30%, there is 77% of probability that the futility boundary is met; if the true ORR is otherwise deemed to be at least 60%, the probability of meeting the boundary is estimated to be $\leqslant$ 2%. Access to the interim results will be limited and the final decision will be made by the SMC along with the sponsor.

8. CHANGES IN THE PLANNED ANALYSIS

Table 4 summarizes the major changes in the planned analyses from the SAP version 1.0 dated on 28 April 2023.

Table 4: Statistical Analysis Plan Changes

Section	Key Change	Rationale of the change
Section 2, Study Overview	Cohort 2 Dose Expansion Stage population was changed to R/R DLBCL patients regardless of PD-L1 expression.	From protocol amendment 2.0, the target population in Cohort 2 dose expansion stage was changed.
Section 6.4.6 Prior and Concomitant medication	Add prior medication. Removed the wording regarding concomitant medication associated with imAE	To clarify the prior medication. The CM association with imAE was removed in protocol amendment 3.
Section 6.6.2 Adverse Events	Clarified the imAE recording time threshold.	It was updated in protocol amendment 3.0.

9. REFERENCES

Brookmeyer R, Crowley J. A confidence interval for the median survival time. Biometrics. 1982;38:29-41.

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Greenwood M. The Natural Duration of Cancer. Reports on Public health and medical subjects. 1926;33:1-26.

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APPENDIX 1. IMPUTATION OF MISSING OR PARTIALLY MISSING DATES

In general, missing or partial dates will not be imputed at the data level. The following rules will apply for the specific analysis and summary purposes mentioned below only.

Prior/Concomitant Medications/Procedures

When the start date or end date of medication is partially missing, the date will be imputed to determine whether the medication is prior or concomitant. The following rules will be applied to impute partial dates for medications:

If the start date of medication is partially missing, impute as follows:

- If both month and day are missing, then set to January 01
- If only day is missing, then set to the first of the month

If the end date of medication is partially missing, impute as follows:

- If both month and day are missing, then set to December 31
- If only day is missing, then set to last day of the month

If start date or end date of medication is completely missing, do not impute. If the imputed of a medication end date > last known alive date or end of study date, then set to the last known alive date or end of study date, whichever occurs first.

Adverse Events

The imputation rule for the safety analyses will be used to address the issues with partial dates. When the start date or end date of an adverse event is partially missing, the date will be imputed to determine whether the adverse event is treatment-emergent. When in doubt, the adverse event will be considered treatment-emergent by default. The following rules will be applied to impute partial dates for adverse events:

If the start date of an adverse event is partially missing, impute as follows:

- If both month and day are missing, then the imputed day and month will be January 01 or the first dosing date if they have the same year, whichever is later.
- If only day is missing, 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 start date is completely missing, the imputed day will be the first dosing date as long as AE end date is not before the first dosing date.

If the end date of an AE is partially missing, impute as follows:

- If both month and day are missing, then set to December 31
- If only day is missing, then set to last day of the month
- If the end date is completely missing, do not impute.

If the imputed AE end date > last known alive date or end of study date, then set to the last known alive date or end of study date, whichever occurs first.

Deaths

In case complete death dates are not recorded, impute as follows:

- If both month and day are missing, then the imputed month and day will be 01Jan or the last date of a patient known to be alive + 1, whichever is later.
- If only day is missing, the death will be assumed to be on the first day of the month or the last date of a patient known to be alive +1, whichever is later.

Subsequent Anti-cancer Therapies

If the start date of a subsequent anti-cancer therapy is incomplete or missing, impute as follows:

- If both month and day are missing, then the imputed month and day will be 01 Jan or the last day of the month for the last adequate disease assessment if they have the same year.
- If only day is missing, then the imputed day will be the first day of the month, or the last day of the month for the last adequate disease assessment if they have the same year and month.

Diagnosis

If a diagnosis date is partially missing, impute as follows:

- If both month and day are missing, then set to January 01
- If only day is missing, then set to the first of the month

If a diagnosis date is completely missing, do not impute.

Prior Therapy/Response to Prior Therapy

If a prior therapy or response to prior therapy date is partially missing, impute as follows:

If start date of a prior therapy is partially missing, impute as follows:

- If both month and day are missing, then set to January 01
- If only day is missing, then set to the first of the month
- If the imputed start date > first dose date then set to the first dose date -1

If end date of a prior therapy is partially missing, impute as follow:

- If both month and day are missing, then set to December 31
- If only day is missing, then set to the last day of the month
- If the imputed end date > first dose date then set to the first dose date -1