STATISTICAL ANALYSIS PLAN

Study Protocol Number:	BGB-LC-203
Study Protocol Title:	A Phase 2, Open-label, Randomized, Multi-arm Study of BGB-A445 in Combination With Investigational Agents in Non-Small Cell Lung Cancer Patients Previously Treated With Anti-PD-(L)1 Antibody
Date:	29 OCT 2024
Version:	1.0
NCT Number:	NCT06029127

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
ADA	antidrug antibody
AE	adverse event
ATC	Anatomical Therapeutic Chemical
BMI	body mass index
BOR	best overall response
CBR	clinical benefit rate
CI	Confidence Interval
CPI	checkpoint inhibitor
CR	complete response
DCR	disease control rate
DOR	duration of response
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
EOT	End-of-Treatment (Visit)
eCRF	electronic case report form
imAE	immune-mediated adverse event
ITT	Intent-to-Treat
LKADT	last known alive date
MedDRA	Medical Dictionary for Regulatory Activities
NCI-CTCAE	National Cancer Institute-Common Terminology Criteria for Adverse Events
NSCLC	non-small cell lung cancer
ORR	overall response rate
OS	overall survival
PD	progressive disease
PD-1	programmed cell death protein-1
PD-L1	programmed death ligand-1

Abbreviation	Definition
PFS	progression-free survival
PK	pharmacokinetic(s)
PR	partial response
PT	Preferred Term
QTcF	QT interval corrected for heart rate using Fridericia's formula
RECIST	Response Evaluation Criteria in Solid Tumors
SAE	serious adverse event
SD	stable disease
SAP	statistical analysis plan
SOC	System Organ Class
TEAE	treatment-emergent adverse event
v	version
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 BGB-LC-203: A Phase 2, Open-label, Randomized, Multi-arm Study of BGB-A445 in Combination With Investigational Agents in Non-Small Cell Lung Cancer Patients Previously Treated With Anti-PD-(L)1 Antibody. The focus of this SAP is for the planned analysis specified in the study protocol. The analysis details for Pharmacogenomics and/or Biomarker analyses are not described within this SAP. Separate analysis plans may be completed for these analyses.

2. STUDY OVERVIEW

This is a Phase 2, open-label, randomized, multicenter, multi-arm study designed to evaluate the efficacy and safety of BGB-A445 in combination with investigational agent(s) in previously treated NSCLC patients whose tumors do not harbor EGFR-sensitizing mutations, ALK translocations, BRAF V600E mutations, RET rearrangement, ROS1 mutations, or another actionable mutation with targeted therapy approved by the local health authority. The patient must not have received more than 2 lines of prior systemic therapies, which must include an anti-PD-(L)1 treatment.

The study is designed to include 2 stages, with the flexibility of adding treatment cohorts when new treatments become available or discontinuing treatment cohorts that demonstrate minimal clinical activity or unacceptable toxicity. In stage 1, patients will be equally enrolled or randomized into different experimental cohorts to receive BGB-A445 plus investigational agent(s). In stage 2, patients will be equally enrolled or randomized into the experimental cohort(s) selected from Stage 1, reference cohort docetaxel + ramucirumab or different dose levels of the investigational agent(s) + BGB-A445 for dose optimization.

3. STUDY OBJECTIVES

3.1. Primary Objective

To assess the antitumor activity of BGB-A445 plus investigational agent(s) in non-small cell lung cancer (NSCLC) patients pretreated with anti-programmed cell death protein 1 (anti-PD-1)/anti-programmed cell death protein ligand 1 (anti-PD-L1) antibody

3.2. Secondary Objective

- To assess the safety and tolerability of BGB-A445 plus investigational agent(s)

- To further assess the antitumor activity of BGB-A445 plus investigational agent(s)

- To characterize the pharmacokinetics (PK) of BGB-A445 and investigational agent(s)

- To assess host immunogenicity to BGB-A445 and investigational protein therapeutics

3.3. Exploratory Objective

- To evaluate the potential association of exploratory biomarkers with response or resistance to study treatment and with patient prognosis

- To further assess the preliminary antitumor activity including by time-to-event of BGB-A445 plus investigational agent(s)

- To assess overall survival (OS)

4. STUDY ENDPOINTS

4.1. Primary Endpoint(s)

Overall response rate (ORR) as assessed by the investigators per Response Evaluation Criteria in Solid Tumors (RECIST) Version (v)1.1.

4.2. Secondary Endpoints

- The incidence and severity of adverse events according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) v5.0 in experimental cohorts (BGB-A445 plus investigational agent)
- Duration of response (DOR), disease control rate (DCR), and clinical benefit rate (CBR) as assessed by the investigator per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1
- Plasma or serum concentrations of BGB-A445 and investigational agents at specified timepoints
- Immunogenic responses to BGB-A445 and investigational protein therapeutics, evaluated through the detection of antidrug antibodies (ADA)

4.3. Exploratory Endpoints

- Evaluate exploratory biomarkers in various sample types (ie, tumor tissue and/or blood) at various timepoints (ie, before study treatment, after study treatment, and/or at disease

progression or recurrence) and the association between these biomarkers and clinical efficacy, disease status, and resistance. Exploratory biomarkers may include, but are not limited to: tumor necrosis factor receptor superfamily, member 4 (CD134, OX40) expression; PD-L1 expression; soluble OX40 (sOX40); investigational agent-specific protein expression; gene expression profiling; tumor-infiltrating immune cells in tumor tissue; tumor mutation burden/microsatellite instability/genetic mutation profiles; circulating tumor DNA (ctDNA), cytokines, and soluble proteins in plasma or serum. Other assessments may be conducted as indicated and as allowed by local regulations.

- Progression-free survival (PFS) as determined from tumor assessments by investigators per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1
- OS defined as the date of randomization to the date of death because of any cause

5. SAMPLE SIZE CONSIDERATIONS

The total number of patients will depend on the number of investigational agents and the timing when they are added to the study. In both Stage 1 and Stage 2, approximately 20 patients will be equally enrolled or randomized into each treatment cohort; approximately 6 patients will be enrolled first if a safety lead-in is planned.

6. STATISTICAL METHODS

In general, data will be summarized by stage, each experimental treatment and/or its concurrent control arm. For a treatment with more than 1 dose levels being evaluated during the trial conduct, comparison between different dose levels will be performed.

6.1. Analysis Sets

The Intent-to-Treat (ITT) Analysis Set consists of all the patients who were enrolled or randomized to a treatment cohort. The ITT Analysis Set will be used as the primary analysis set for efficacy and patient characteristics unless specified otherwise.

The Safety Analysis Set consists of all the patients who were enrolled or randomized and received any dose of any study drug. The safety analysis set is used for all safety and exposure analyses.

The Efficacy Evaluable Analysis Set consists of all patients who were enrolled or randomized and received any dose of any study drug, have evaluable disease at baseline, and have ≥ 1 evaluable postbaseline tumor response assessment unless any clinical progressive disease or

death occurred before the first postbaseline tumor assessment. The Efficacy Evaluable Analysis Set will be used as the supportive analysis population for efficacy endpoints.

The clinical disease progression is identified by the study treatment discontinuation due to progressive disease without radiographic confirmation before the first postbaseline tumor assessment.

The PK Analysis Set consists of all the patients who received any dose of the study drug and for whom the valid study drug PK parameters can be estimated.

The ADA (antidrug antibody) Analysis Set includes all patients who received the study drug(s) and in whom both baseline ADA and ≥ 1 postbaseline ADA results are available.

6.2. Multiplicity Adjustment

Since no formal hypothesis is tested in this study, multiplicity adjustment is not needed.

6.3. Data Analysis General Considerations

6.3.1. Definitions and Computations

Study day will be calculated in reference to the baseline date, e.g. the date of the first dose of any study drug(s). For assessments conducted on or after the baseline date, the study day will be calculated as (assessment date – the baseline date + 1). For assessments conducted before the baseline date, study day is calculated as (assessment date – the baseline date). 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 or on baseline date.

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

6.3.2. Conventions

No formal hypothesis will be tested in this study. Data will be mainly analyzed descriptively. Confidence intervals (CIs) will be constructed to describe the precision of the point estimates of interest (e.g., objective response rate and disease control rate).

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 decimal place.
- 1 month = 30.4375 days. Number of months is calculated as (days/30.4375) rounded up to 1 decimal place.
- Duration of image-based event endpoints (such as PFS and DFS) 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. Specific rules are provided in Appendix 1.

By-visit endpoints will be analyzed using observed data unless otherwise specified.

6.4. Patient Characteristics

Patient characteristics will be presented in the ITT analysis set.

6.4.1. Patient Disposition

The number (percentage) of patients treated, discontinued from treatment, discontinued from study, reasons of treatment discontinuation, reasons of study discontinuation, and the duration of study follow-up will be summarized.

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. 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, including the following variables:

- Age (continuously and by categories [< 65 or ≥ 65 years])
- Sex
- Race
- Ethnicity
- Height
- Weight
- BMI
- ECOG at baseline
- Time from initial diagnosis to study entry

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. Disease characteristics include:

- AJCC stage at study entry
- AJCC stage at initial diagnosis
- Metastatic disease at study entry

- Known metastatic site at initial diagnosis
- Histology classification
- Histologic grade

A listing of disease history will be provided.

6.4.5. Prior Anticancer Therapy

Prior anticancer systemic therapies and radiation therapies will be summarized. The variables include:

For prior anticancer systemic therapy:

- number of patients with any prior anticancer systemic therapy
- number of prior lines of anticancer systemic therapy

For prior radiotherapy:

- number of patients with any prior radiotherapy

6.4.6. Prior and Concomitant Medications

Prior medications are defined as medications that stopped before the first dose of any study drug. Concomitant medications will be defined as medications that 1) started before the first dose of study drug and were continuing at the time of the first dose of study drug, or 2) started on or after the date of the first dose of study drug up to 30 days after the patient's last dose (as of the EOT/Safety Follow-up Visit). In addition, relevant concomitant medications/procedures (if appropriate, ie, associated with an immune-mediated adverse event) within 90 days (± 14 days) after the last dose of study treatment(s) may also be included as part of the analysis.

Prior and concomitant medications will be coded using the version of World Health Organization Drug Dictionary (WHO DD) drug codes currently in effect at BeiGene. 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. 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 27.0 or higher. 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. A listing of medical history will be provided.

6.5. Efficacy Analysis

6.5.1. Primary Efficacy Endpoint

The best overall response (BOR) is defined as the best response recorded from the date of randomization until progressive disease (PD), death, cut-off date, or initiation of new anticancer therapy, whichever comes first. If the first tumor assessment occurs after the new anticancer therapy, the BOR is considered as NE.

Objective Response Rate (ORR) is defined as the proportion of patients with best overall response (BOR) of a confirmed CR or PR. Patients in the refence population without confirmed CR or PR including those with missing or NE tumor assessments will be counted as non-responders. ORR based on unconfirmed PR or CR will also be summarized. ORR will be analyzed in the ITT analysis set and efficacy evaluable analysis set.

More detail about the RECIST Version (v)1.1 can be found in Appendix 5 of the protocol BGB-LC-203.

The ORR will be summarized with descriptive statistics and the corresponding two-sided 95% CIs calculated from Clopper Pearson exact method. Further rules for the primary analysis of ORR are presented in Table 1. In Stage 2, the ORR difference between any experimental cohort and the concurrent reference cohort (Δ ORR) and the corresponding 95% CIs will be reported.

Table 1: Handling of Intercurrent Events and Missing Values for the Primary Analysis of ORR

	Derivation rules
Intercurrent events	
New anticancer therapy started prior to disease progression or death	Patients starting any new anticancer therapy without achieving a CR or PR before will be considered as non-responders (composite strategy)
Discontinuation of treatment prior to disease progression or death	Response assessment after discontinuation of treatment will be counted and used for analysis (treatment policy strategy)

Missing values not related to intercurrent events	
No post-baseline response assessment (regardless of the reason)	Non-responders

Refer to the following for more detailed definition of BOR:

- Confirmed Complete Response (CR) per RECIST v1.1 is defined as at least 4 weeks apart (in-between) 2 CRs. Single "Unevaluable (NE)" between two CRs, (CR NE CR) is considered as confirmed CR. More than one NE between CR is considered as unconfirmed.
- Confirmed Partial Response (PR) per RECIST v1.1 is defined as at least 4 weeks apart (in-between) the first PR and the last PR/CR. Single "NE" or "SD" between two PRs, (PR NE PR, or PR SD PR) is considered as confirmed. More than one NE/SD after PR is considered as unconfirmed.
- Durable Stable Disease (SD) per RECIST v1.1, is defined as the assessments of SD which is at least 5 weeks after the randomization date.
- For the best overall response, the priority of response reported would be CR over PR over SD over Progressive disease over Could Not Be Determined.

6.5.2. Secondary and Exploratory Efficacy Endpoints

The secondary and exploratory efficacy endpoints include DOR, DCR, CBR, PFS and OS by investigators per RECIST v.1.1.

DCR and CBR

DCR is defined as the proportion of patients with BOR of a CR, PR, or stable disease. CBR is defined as the proportion of patients with BOR of a CR, PR, or stable disease lasting ≥ 24 weeks. The CBR and DCR will be analyzed similarly to ORR. In addition, the difference between any experimental cohort and the reference cohort will be reported in Stage 2.

PFS

PFS is defined as the time from the date of randomization to the date of the first documentation of disease progression or death due to any cause, whichever occurs first. PFS analysis will be conducted in the ITT analysis set. The distribution of PFS, including median, Q1 and Q3 will be estimated using the Kaplan-Meier method for each treatment group. Ninety-five percent CIs for

median and Q1 and Q3 of PFS will be estimated using the method of Brookmeyer and Crowley (Brookmeyer and Crowley, 1982).

The censoring rules for the primary analysis of PFS are presented in Table 2: Handling of Intercurrent Events and Missing Values of Progression-free Survival Per RECIST Version 1.1 2.

Table 2: Handling of Intercurrent Events and Missing Values of Progression-free Survival Per RECIST Version 1.1

	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
Intercurrent events		
Discontinuation of the treatment	Tumor assessment data collected after discontinuation of study treatment will be used for analysis (treatment policy strategy)	No impact
New anticancer therapy started prior to disease progression or death	Last adequate disease assessment before the new anticancer therapy (hypothetical strategy)	Censored
Missing values not related to intercurrent events		
Patients' withdrawal from the study or lost to follow-up	Last adequate disease assessment prior to patients' withdrawal from the study (hypothetical strategy)	Censored
No baseline or any post-baseline tumor assessments without death	Date of randomization	Censored
No baseline or any post-baseline tumor assessments with death (within 13 weeks or 91 days from the date of randomization)	Date of death	Event
Death or progression after more than one missed visit	Date of last adequate radiologic assessment before missed tumor assessments	Censored

A patient meets the criteria for more than 1 censoring rules above	Date of the earliest censoring date among all events	Censored

Duration of Response (DOR)

DOR is defined as the time from the first determination of an objective response until the first documentation of progression or death due to any cause, whichever occurs first. Duration of response analysis will only include responders. The censoring rule for DOR will follow the PFS censoring rule (see above Table 2: Handling of Intercurrent Events and Missing Values of Progression-free Survival Per RECIST Version 1.1

2). Kaplan Meier methodology will be used to estimate the Q1, Q3 and median duration, and the 95% confidence interval for the duration of response will be provided.

Overall Survival (OS)

OS is defined as time from the date of randomization to the date of death for patients who died prior to or on the cutoff date. OS analysis will be conducted in the ITT analysis set. For patients who are alive by the cutoff date, OS will be censored at the last known alive date (LKADT). For patient are still on treatment at cutoff date, the LKADT will be defined as data cutoff date. For patient who discontinue treatment but still alive, the LKADT will be defined as last known alive date or cutoff date whichever comes first.

The distribution of OS, including median, Q1 and Q3 will be estimated using the Kaplan-Meier method for each treatment group. Ninety-five percent CIs for median and Q1 and Q3 of OS will be estimated using the method of Brookmeyer and Crowley (Brookmeyer and Crowley, 1982).

The censoring rules for OS are presented in Table 3:Handling of Intercurrent Events and Missing Values for the Primary Analysis of Overall Survival

Table 3: Handling of Intercurrent Events and Missing Values for the Primary Analysis of Overall Survival

	Derivation rules	**Outcome**
Intercurrent events		
Discontinuation of the treatment	Tumor assessment data collected after discontinuation of study treatment will be used for analysis (treatment policy strategy)	No impact

New anticancer therapy started prior to death	Ignored (treatment policy strategy)	No impact
Missing values not related to intercurrent events		
Patients' withdrawal from the study or lost to follow-up	Last known alive date prior to withdrawal. (hypothetical strategy)	Censored
Missing visits	Ignored	No impact

6.5.3. Subgroup Analyses

Efficacy endpoints, including ORR, DCR and CBR, will be analyzed by checkpoint inhibitor (CPI) resistance status. Patients will be categorized into the following groups according to their CPI resistance status: 1) Primary resistance: patients who did not respond to previous CPI treatment; 2) Acquired resistance: patients who responded to previous CPI treatment but progressed before joining this study; 3) Unknown: response to previous CPI treatment is missing.

6.6. Safety Analyses

The safety profile will be determined by reporting of AEs and by laboratory values. Vital signs and ECG findings will also be used in determining the safety profile. The severity of AEs will be graded according to NCI-CTCAE v5.0. The incidence of TEAEs will be reported as the number (percentage) of patients with TEAEs by MedDRA system organ class and preferred term. Descriptive summary statistics (eg, n, mean, standard deviation, median, minimum, and maximum for continuous variables; n [%] for categorical variables) and changes from baseline will be determined for vital signs.

Safety data will be summarized using the safety analysis set.

6.6.1. Extent of Exposure

The following measures of the extent of exposure will be summarized:

Residual days of the last dose is defined based on the planned dose schedule in the protocol.

For A445, Docetaxel and Ramucirumab, the infusion cycle is 21 days. The days to be covered by the last dose is defined as the last infusion date + 20 days.

The dosing schedule of 15025 is QD, so the days to be covered by the last dose would be 0.

Calculation For individual drugs:

Treatment duration (in months) = treatment duration end date – first dose date + 1, where the treatment duration end date is defined as cutoff date for patients with treatment ongoing, and min (cutoff date, death date, last dose date + residual days of the last dose) for patients who discontinue the treatment.

Calculation For combination therapies:

The treatment duration for the combination therapy = the treatment duration end date of the combination therapy – the treatment duration start date of the combination therapy + 1, where the treatment duration end date of the combination therapy is the latest of the treatment duration end date of the individual drug as defined in the previous section and the treatment duration start date of the combination therapy is the earliest of first dose date of the individual drug.

Exposure Summary Statistics:

The following information related to exposure will be provided for each study drug.

- Duration of exposure
- Number of cycles received: defined as the total number of treatment cycles in which at least one dose of the study drug is administered.
- Cumulative dose administered (mg)
- Actual dose intensity: defined as the total dose received by a patient divided by last dose date up to cutoff date + residual days of the last dose – first dose date + 1.
  - For A445, the unit is mg/cycle.
  - For 15025, the unit is mg/day
  - For Docetaxel, the unit is mg/m^2/cycle
  - For Ramucirumab, the unit is mg/kg/cycle
    - The dose of docetaxel (mg) will be calculated based on body surface area (BSA) with BSA(m^2) = 0.0061×Height(cm)+0.0128×weight(kg) - 0.1529
    - To calculate the dose of Ramucirumab (mg) and Docetaxel (mg), baseline weight will be used unless weight change for one visit is at least 10% greater compared to baseline weight.
- Relative dose intensity (%): defined as the ratio of the actual dose intensity and the planned dose intensity. Planned dose intensity is defined as the planned dose intensity on study day 1.

- Number (%) of patients with dose modification and number of dose modifications per patient
- Number (%) of patients with any dose reduction and number of dose reductions per patient
- Number (%) of patients with any dose delay and number of dose delay per patient (A445, Docetaxel and Ramucirumab)
- Number (%) of patients with any infusion interruption and number of infusion interruption per patient (A445, Docetaxel and Ramucirumab)
- Number (%) of patients with any dosing error and number of dosing error per patient (15025)
- Reasons for dose modifications
- Reasons for dose reductions
- Reasons for dose delays (A445, Docetaxel and Ramucirumab)
- Reasons for infusion interruptions (A445, Docetaxel and Ramucirumab)

Patient data listings will be provided for all dosing records.

6.6.2. Adverse Events

AEs will be graded by investigators using CTCAE version 5.0 or higher. 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 27.0 or higher) lower 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 or increase in severity level date on or after the date of the first dose of study drug and up to 30 days after the last dose of study drug(s) or the initiation of new anti-cancer therapy, whichever is earlier.

An immune-mediated adverse event (imAE) is defined as an adverse event within 90 days of the last dose of study treatment and for which a coded MedDRA PT meets imAE criteria based on Company Custom Queries (CCQ) Version 3.0 or higher, as summarized in Appendix 2.

Summary tables will generally focus on those TEAEs or imAE. All AEs, treatment emergent or otherwise, will be presented in patient data listings.

A TEAE overview table, including the number and percentage of patients with 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 lead to dose modification, TEAEs leading to dose modification such as dose reduction and dose interruption, corresponding treatment-related TEAEs, dose limiting toxicity and infusion-related reactions will be provided.

Treatment-related AEs include those events considered by the investigator reported in CRF or with a missing assessment of the causal relationship.

The incidence of TEAEs will be reported as the number (percentage) of patients with TEAEs by SOC and PT. 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. The number (percentage) of patients with treatment-related TEAEs, TEAEs with grade 3 or above, SAEs, TEAEs that led to death, and TEAEs that led to treatment discontinuation, modification will be summarized by SOC and PT. Additionally, the number (percentage) of patients with treatment-emergent hematologic event and outcome of treatment-emergent hematologic event for A445+Docetaxel arm will also be provided.

An imAE overview table, including the number of percentage of patients with imAEs, serious imAE, imAE with Grade 3 or above, imAE that led to death, imAE that led to treatment discontinuation, imAE that led to treatment modification, imAE that treated with systemic corticosteroids, hormone therapy and other immunosuppressant will be provided. imAEs will also be summarized by Category and PT.

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

6.6.3. Laboratory Values

Hematology lab parameters that are graded in NCI CTCAE Version 5.0 will be summarized by shifts from baseline CTCAE grades to maximum post-baseline grades. Laboratory parameters of potential Hy's law will also be summarized. Patient data listings of hematology laboratory abnormalities will be provided.

6.6.4. Vital Signs

Vital sign parameters, including systolic and diastolic blood pressure, pulse rate, temperature, and weight will be presented by subjects and visits in a listing.

6.6.5. Electrocardiograms (ECG)

ECG will be performed during baseline and multiple time post-baseline points (refer the time points to the protocol study assessments and procedures schedule). Postbaseline abnormal QTcF observations will be summarized, including:

- Numbers of patients with any postbaseline QTcF greater than 450, 480 and 500 milliseconds
- Numbers of patients with any postbaseline QTcF increase of more than 30 and 60 milliseconds compared to the baseline QTcF

6.7. Pharmacokinetic Analyses

Serum/plasma concentration data will be tabulated and summarized by the visit/cycle at which these samples are collected. Descriptive statistics will include means, medians, ranges, and standard deviations, as appropriate.

6.8. Immunogenicity Analyses

ADA samples will be collected for BGB-A445 and relevant investigational agents in this study. The immunogenicity results will be summarized using descriptive statistics by the number and percentage of patients who develop detectable ADAs. The incidence of positive ADAs and neutralizing ADAs will be reported for evaluable patients.

7. INTERIM ANALYSES

A futility analysis will be conducted when approximately 20 patients are enrolled or randomized in any of the experimental cohorts at the end of Stage 1 and when these patients have been followed up for $\geqslant$ 2 postbaseline tumor assessments. Bayesian posterior probability will be used to evaluate clinical antitumor activity in Stage 1 for BGB-A445 in combination with investigational agents in each cohort. An experimental cohort will be considered futile and not proceed to Stage 2 if the ORR in this group is unlikely to exceed a historical benchmark (eg, Posterior Probability [true ORR $\geqslant$ 23%] $\leqslant$ 20%). The historical benchmark will be assessed periodically and may be updated based on the emergent data during the cause of the study.

8. CHANGES IN THE PLANNED ANALYSIS

The ADA (antidrug antibody) Analysis Set will be added for ADA analysis.

9. REFERENCES

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

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.

1. **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.

2. **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.

known alive date or end of study date, whichever occurs first.

3. **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 January 01 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.

4. **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 set to December 31
- If only day is missing, then set to last day of the month
- If the imputed start date > min (death date, study discontinuation date, data cutoff date, start date of the subsequent anti-cancer therapy), then set to min (death date, study discontinuation date, data cutoff date, start date of the next subsequent therapy)

5. **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.

APPENDIX 2. imAE DEFINITION

An immune-mediated adverse event is defined as an adverse event within 90 days of the last dose of study treatment and for which a coded MedDRA PT meets 1 of 2 components below:

- A narrow list of PTs from the immune-mediated adverse event CCQ v3.0 or higher for which the immune-mediated etiology is specified within the PT itself are always considered to be immune-mediated adverse events (eg, immune-mediated hypothyroidism).
- A broad list of PTs from the immune-mediated adverse event CCQ v3.0 or higher that are known or possible immune-mediated adverse events, and that are considered immune-mediated adverse events when any of the following additional criteria are met (if applicable):
  - Investigator causality assessment reported as related to any study drug
  - Investigator assessment reported as an immune-mediated adverse event in the case report form
  - Action taken with any study drug as drug interruption or drug discontinuation
  - Treatment of the adverse event with systemic corticosteroids or other immunosuppressants
  - Treatment of adverse events from the categories of immune-mediated hypothyroidism, hyperthyroidism, and thyroiditis with thyroid replacement/antithyroid agents
  - Treatment of adverse events from the category of immune-mediated type 1 diabetes mellitus treated with insulin