

DISCLOSURE

REDACTED STATISTICAL ANALYSIS PLAN

BGB-A317-NSCL-001 and BGB-A317-NSCL-001C

A PHASE 3, RANDOMIZED, BLINDED, PLACEBO-CONTROLLED STUDY OF TISLELIZUMAB (BGB-A317) PLUS CHEMORADIOTHERAPY FOLLOWED BY TISLELIZUMAB MONOTHERAPY IN NEWLY DIAGNOSED, STAGE III SUBJECTS WITH LOCALLY ADVANCED, UNRESECTABLE NON-SMALL CELL LUNG CANCER

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STATISTICAL ANALYSIS PLAN

A PHASE 3, RANDOMIZED, BLINDED, PLACEBO-CONTROLLED STUDY
OF TISLELIZUMAB (BGB-A317) PLUS CHEMORADIOTHERAPY
FOLLOWED BY TISLELIZUMAB MONOTHERAPY IN NEWLY
DIAGNOSED, STAGE III SUBJECTS WITH LOCALLY ADVANCED,
UNRESECTABLE NON-SMALL CELL LUNG CANCER

STUDY DRUG: TISLELIZUMAB (BGB-A317)

PROTOCOL NUMBER: BGB-A317-NSCL-001 and BGB-A317-NSCL-001C

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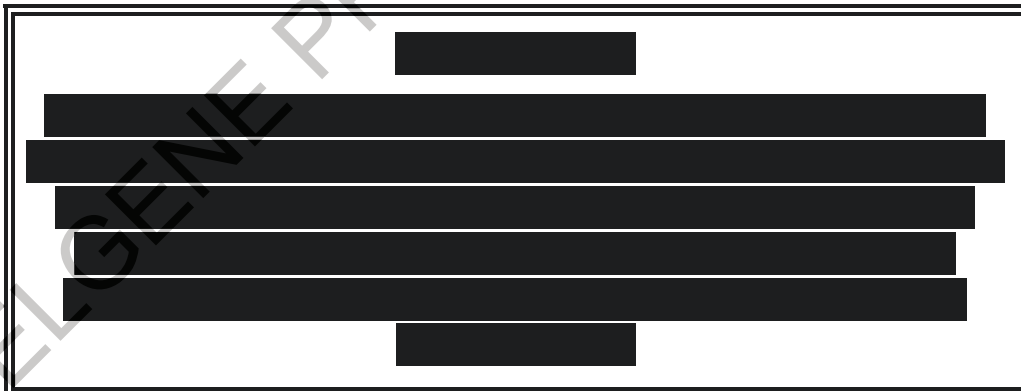


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CCI [REDACTED]

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SIGNATURE PAGE

STATISTICAL ANALYSIS PLAN (SAP) AND SAP AMENDMENT APPROVAL SIGNATURE PAGE	
SAP TITLE	BGB-A317-NSCL-001 and BGB-A317-NSCL-001C Statistical Analysis Plan
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SAP AUTHOR	PPD
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PROTOCOL VERSION, DATE	BGB-A317-NSCL-001: Amendment 1, 20-Sep-2018; BGB-A317-NSCL-001C: Final, 03-Oct-2018
SIGNATURE STATEMENT	By my signature, I indicate I have reviewed this SAP and find its contents to be acceptable.
Statistical Therapeutic Area Head	
Signature	<u><i>{See appended electronic signature page}</i></u>
Printed Name	_____ Date _____
Lead Clinical Research Physician / Clinical Research Physician	
Signature	<u><i>{See appended electronic signature page}</i></u>
Printed Name	_____ Date _____
Lead Product Safety Physician	
Signature	<u><i>{See appended electronic signature page}</i></u>
Printed Name	_____ Date _____

1. LIST OF ABBREVIATIONS

Table 1: Abbreviations and Specialist Terms

ADA	Antidrug antibodies
AE	Adverse event
ALT	Alanine aminotransferase (SGPT)
ANC	Absolute neutrophil count
APF12	Alive and progression free at 12 months
APF18	Alive and progression free at 18 months
AST	Aspartate aminotransferase (SGOT)
AUC	Area under the curve
cCRT	Concurrent chemoradiotherapy
BMI	Body mass index
BSA	Body surface area
CI	Confidence interval
CMH	Cochran-Mantel-Haenszel
CR	Complete response
CRF	Case report form
CT	Computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
DNA	Deoxyribonucleic acid
DOR	Duration of response
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
EGFR	Epidermal growth factor receptor
EORTC QLQ-C30	European organisation for research and treatment of cancer - quality of life C30 questionnaire
EORTC QLQ-LC13	European organisation for research and treatment of cancer - quality of life C30 questionnaire lung cancer module
EOT	End of treatment

CCI

FDA	Food and Drug Administration
HR	Hazard ratio
HRQoL	Health-related quality of life
IDMC	Independent data monitoring committee
IFN- γ	Interferon- γ
IRT	Interactive response technology
ITT	Intent-to-treat
IV	Intravenous
LDH	Lactic dehydrogenase
MedDRA	Medical Dictionary for Regulatory Activities
MRI	Magnetic resonance imaging
NA	Not applicable
NCI	National Cancer Institute
NSCLC	Non-small cell lung cancer
ORR	Objective response rate
OS	Overall survival
PD	Progressive disease
PD-L1	Programmed cell death protein-ligand 1
PFS	Progression-free survival
PK	Pharmacokinetic
PP	Per protocol
PR	Partial response
PRO	Patient-reported outcome
RECIST	Response Evaluation Criteria in Solid Tumors
RNA	Ribonucleic acid
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Stable disease

STDEV	Standard deviation
Q3W	Every 3 weeks
SGOT	Serum glutamic oxaloacetic transaminase (AST)
TEAE	Treatment-emergent adverse events
TEirAE	Treatment-emergent immune-related adverse event
CCI	[REDACTED]
SGPT	Serum glutamic pyruvic transaminase (ALT)
TTDM	Time to death or distant metastasis
NE	Not-evaluable

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2. INTRODUCTION

This Phase 3 study will be conducted under 2 protocols as follows:

- 1) Protocol BGB-A317-NSCL-001 is the main protocol
- 2) Protocol BGB-A317-NSCL-001C is the companion protocol

The protocols BGB-A317-NSCL-001 and BGB-A317-NSCL-001C have a total combined enrollment target of 840 subjects utilizing a virtually identical study design and patient population with regards to inclusion and exclusion criteria. Both study protocols will utilize one IRT (Interactive Response Technology) for stratification and randomization and the data from two protocols will be collected into a single database. All the statistical analyses as described in this statistical analysis plan (SAP) will be performed on the combined total number of subjects randomized into either the main protocol or the companion protocol as one study. A single independent data monitoring committee (IDMC) and blinded independent central review will be utilized for these 2 protocols. There are minor differences, primarily administrative in nature, between the

This SAP describes the analyses and data presentations for Celgene's protocols BGB-A317-NSCL-001 and BGB-A317-NSCL-001C "A PHASE 3, RANDOMIZED, BLINDED, PLACEBO-CONTROLLED STUDY OF TISLELIZUMAB (BGB-A317) PLUS CHEMORADIOTHERAPY FOLLOWED BY TISLELIZUMAB MONOTHERAPY IN NEWLY DIAGNOSED, STAGE III SUBJECTS WITH LOCALLY ADVANCED, UNRESECTABLE NON-SMALL CELL LUNG CANCER". Protocol BGB-A317-NSCL-001 was originally issued on 21May2018 and subsequently amended on 20Sep2018 (Amendment No. 1). Protocol BGB-A317-NSCL-001C was originally issued on 03Oct2018. The two protocols contain the same definitions of analysis populations, derived variables and statistical methods for the analysis of efficacy and safety, which are defined in this SAP.

There will be one interim and one final analysis for progression-free survival (PFS), and one interim and one final analysis for overall survival (OS), respectively. The interim OS analysis will occur at the same as the final PFS analysis. Therefore, there will be 3 data cutoff time points in this study:

CCI [REDACTED]

Celgene anticipates accrual will be completed before the interim analysis of PFS is performed and the study is planned to continue until completion of the final PFS and OS analyses.

Throughout this SAP, the treatment arms will be referred to as the following 3 arms:

- 1. [REDACTED]
- 2. [REDACTED]
- 3. [REDACTED]
- 4. [REDACTED]
- 5. [REDACTED]

The purpose of the SAP is to ensure the credibility of the study findings by pre-specifying the statistical approaches to the analysis of study data prior to database lock and any data analysis for the interim analysis. This SAP will be finalized and signed prior to the clinical database lock for the interim analysis of PFS. All statistical analyses detailed in this SAP will be conducted using SAS® Version 9.4 or higher.

The decision of closing the study in very early stage is leading to the decision not to conduct any planned statistical analysis. As a consequence, the SAP is remaining in this draft version. The changes in the planned analysis are presented in section 16.

3. STUDY OBJECTIVES

3.1. Primary Objective

The primary objective is to compare the PFS of tislelizumab in combination with cCRT followed by tislelizumab monotherapy (Arm 1) versus cCRT alone (Arm 3); in addition, tislelizumab given sequentially after cCRT (Arm 2) will be compared with cCRT alone (Arm 3) in newly diagnosed stage III subjects with locally advanced unresectable non-small cell lung cancer (NSCLC).

3.2. Secondary Objectives

The secondary objectives are to:

- Compare OS (key secondary objective)
- Compare OS at 24 months (key secondary objective)
- Compare centrally-assessed objective response rate (ORR) (key secondary objective)
- Compare centrally-assessed duration of response (DOR)
- Compare proportion of subjects alive and progression-free at 12 and 18 months (APF12, APF18)
- Compare time to death or distant metastasis (TTDM)
- Compare safety and tolerability of tislelizumab in combination with cCRT followed by tislelizumab monotherapy versus cCRT alone, and tislelizumab given sequentially after cCRT versus cCRT alone.
- Compare impact on patient-reported lung cancer symptoms (appetite loss, cough, chest pain, dyspnea, and fatigue) assessed by European Organisation for Research and Treatment of Cancer – Quality of Life C30 questionnaire (EORTC QLQ-C30) and its lung cancer module (EORTC QLQ-LC13).
- Compare the proportion of subjects who received at least one dose of tislelizumab or placebo in the monotherapy phase before progression in Arm 1 versus Arm 2 and 3.

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4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This Phase 3 study will be conducted under 2 protocols as follows:

- 1) Protocol BGB-A317-NSCL-001 is the main protocol [REDACTED]
- 2) Protocol BGB-A317-NSCL-001C is the companion protocol [REDACTED]

It is important to note that these 2 protocols BGB-A317-NSCL-001 and BGB-A317-NSCL-001C constitute a single global Phase 3, randomized, double-blind, placebo-controlled multicenter study designed to compare the efficacy and safety of tislelizumab in combination with concurrent chemoradiotherapy (cCRT) followed by tislelizumab monotherapy versus cCRT alone, and tislelizumab given sequentially after cCRT versus cCRT alone, in newly diagnosed stage III subjects with locally advanced, unresectable NSCLC.

The primary endpoint is centrally-assessed PFS in the intent-to-treat (ITT) population. Newly diagnosed stage III subjects with histologically confirmed, locally advanced, unresectable NSCLC are eligible.

The two protocols BGB-A317-NSCL-001 and BGB-A317-NSCL-001C have a total combined enrollment target of approximately 840 subjects who will be randomized in a 1:1:1 ratio to receive the study drug

tislelizumab or placebo in one of the following 3 treatment arms:

- CCI [REDACTED]

The choice of chemotherapy regimen to be used as part of study treatment will be at the Investigator's discretion, consisting of either 2 cycles of cisplatin plus etoposide or weekly carboplatin plus paclitaxel given during radiation therapy (RT) for 6 weeks. Radiation therapy should start concurrently with chemotherapy in Cycle 1 of tislelizumab or placebo. If local technical or logistical circumstances do not allow for the start of RT at the beginning of Cycle 1, a 3-day administrative window to start RT will be allowed. Tislelizumab or placebo will be given starting from Cycle 1 Day 1 (C1D1) in the cCRT phase, and continued in the monotherapy phase for a duration of 12 months following the completion of cCRT, or until disease progression, unacceptable toxicity, or treatment discontinuation for another reason.

Randomization will be stratified by age (CCI [REDACTED]), chemotherapy regimen

CCI [REDACTED], and region CCI [REDACTED]
[REDACTED]

Safety and efficacy will be monitored by an IDMC. There will be IDMC safety assessments during which the IDMC will examine unblinded safety data including but not limited to serious adverse events (SAEs), adverse events, and other safety data individually and in aggregate, and will provide recommendations on the continuation of the 3 arms based on safety and tolerability. The first IDMC safety assessment will be conducted after approximately 30 subjects CCI [REDACTED]

[REDACTED]. The second IDMC safety assessment will be conducted as determined by the IDMC but no later than 3 to 6 months after the first evaluation. Subsequent assessments will take place approximately every 6 months thereafter. CCI [REDACTED]

[REDACTED] Enrollment may continue during these IDMC safety reviews.

Full details of the IDMC procedures and processes can be found in the IDMC Charter. For immune therapies such as tislelizumab, pseudoprogression may occur due to immune-cell infiltration and other mechanisms, leading to apparent increase of existing tumor masses or appearance of new tumor lesions. Thus, if radiographic progressive disease is suspected by the Investigator to reflect pseudoprogression, the subject may continue treatment until progressive disease is confirmed by repeated imaging at least 4 weeks later but not exceeding 6 to 8 weeks from the date of initial documentation of progressive disease, provided the following criteria are met:

- Absence of clinical symptoms and signs of disease progression (including clinically significant worsening of laboratory values).
- Stable ECOG performance status (≤ 1).
- Absence of rapid progression of disease or of progressive tumor at critical anatomical sites (eg, cord compression) that requires urgent alternative medical intervention.

Investigators must obtain written informed consent for treatment beyond radiologic disease progression and inform subjects that this practice is not considered standard in the treatment of cancer. The decision to continue study drug(s) beyond initial Investigator-assessed progression must be discussed with the Sponsor medical monitor and documented in the study records.

The study conduct will be overseen by a Steering Committee (SC) composed of selected Investigators who are taking part in the study. The SC will remain blinded to the study data by arm.

The study will be conducted in compliance with International Council for Harmonisation (ICH) Good Clinical Practices (GCPs).

The study schematic is presented in 18.1.

4.2. Study Endpoints

4.2.1. Primary Efficacy Endpoint(s)

The primary endpoint is PFS, defined as the time from the date of randomization to the date of the first objectively documented tumor progression as assessed by blinded independent central review per RECIST v1.1 or death from any cause, whichever occurs first.

4.2.2. Secondary Endpoints

4.2.2.1 Key Secondary Endpoints

- OS, defined as the time from the date of randomization to the date of death due to any cause
- OS at 24 months, defined as the proportion of subjects alive at 24 months after randomization.
- ORR defined as the proportion of subjects who had complete response (CR) or partial response (PR) as assessed by blinded independent central review per RECIST v1.1

4.2.2.2 Other Secondary Endpoints

- The time from the first occurrence of a documented objective response to the time of relapse, as determined by blinded independent central review per RECIST v1.1, or death from any cause, whichever comes first
- The proportion of subjects alive and progression free at 12 months (APF12) will be defined as the Kaplan-Meier estimate of PFS at 12 months
- The proportion of subjects alive and progression free at 18 months (APF18)
- TTDM will be defined as the time from the date of randomization until the first date of distant metastasis or death in the absence of distant metastasis. Distant metastasis is defined as any new lesion that is outside of the radiation field according to RECIST v1.1 or proven by biopsy
- Safety and tolerability will be assessed from adverse events (using NCI CTCAE v5.0), laboratory tests, vital signs, ECOG performance status, physical exams, concomitant medications, and dose modifications
- Differences between study arms, tests for within-group changes over time and tests for both deterioration and improvement will be performed on the selected lung cancer symptoms (appetite –item 13 of EORTC QLQ-C30, cough – items 31 of EORTC QLQ-LC13, haemoptysis – item 32 of EORTC QLQ-LC13, chest pain – item 40 of EORTC QLQ-LC13, dyspnea –items 33 to 35 of EORTC QLQ-LC13, and fatigue – items 10, 12, 18 of EORTC QLQ-C30), and physical functioning – items 1 to 5 of EORTC QLQ-C30.
- Proportion of subjects who receive at least one dose of tislelizumab or placebo in the monotherapy phase before progression as determined by blinded independent central review per RECIST v1.1

CCI

[REDACTED]

[REDACTED]

4.3. Stratification, Randomization, and Blinding

4.3.1. Randomization and Stratification

Subjects who enter screening will be assigned the next available subject number. All eligible subjects will be randomized by IRT via 1:1:1 ratio to one of the following treatment arms:

CCI
[REDACTED]

The permuted block randomization method will be used to generate the randomization codes and the randomization will be performed by IRT to ensure a 1:1:1 treatment assignment ratio. The

[REDACTED]

randomization schedule will be generated by the Sponsor or its designee. The randomization will be stratified by age [redacted], chemotherapy regimen [redacted], and region [redacted]).

4.3.2. Blinding

This is a randomized, double-blind, Phase 3 study. Subjects will be randomized to receive tislelizumab or placebo in a double-blind fashion. Investigators, subjects, and researchers will be remaining in blinded throughout entire study until database lock. An independent statistics and programming team will perform unblinding interim analyses and DMC data analysis.

4.4. Sample Size Determination

There are 2 primary hypotheses in this study:

- H1: PFS in Arm 1 \leq Arm 3 versus PFS in Arm 1 $>$ Arm 3
- H2: PFS in Arm 2 \leq Arm 3 versus PFS in Arm 2 $>$ Arm 3

[redacted]

The median PFS in the control arm (Arm 3) was based on data from historical trials with similar patients. Ahn (2015) ([Ahn, 2015](#)) and Belderbos (2007) ([Belderbos, 2007](#)) reported that the median PFS for inoperable (unresectable) stage III NSCLC treated with concurrent chemo-radiotherapy are 8.1 months and 8.5 months, respectively. Factoring in potential improvements in best supportive care, Celgene used a [redacted] estimate for median PFS of 9 months for the control arm for the sample size and power calculation.

For the target PFS treatment effect, Celgene considered a hazard ratio of 0.7 as a clinically meaningful improvement of PFS and used that for the sample size and power calculation. This target is considered reasonable based on cross-trial evaluation of historical data for cCRT described above, including that from the recently published PACIFIC study results ([Antonia, 2017](#)). Celgene considers T0 as PFS from cCRT treatment and T1 as PFS from anti-PD-1 consolidation (durvalumab) treatment for patients who have stable disease or better following cCRT. Heuristically, Celgene approximates the cCRT + anti-PD-1 PFS as $T = T0(T0 \leq 2) + (2 + T1)(T0 > 2)$ for first line treatment. Fitting historical medians of T0 and T1, 8 and 16.8 months respectively, and conducting simulations, the median PFS is close to 14.6 months, which corresponds to an approximately 38% improvement consistent with the target hazard ratio of 0.7.

A similar assessment was performed for OS. The median OS in the control arm was estimated at 22 months from Ahn (2015) ([Aha, 2015](#)). [REDACTED]

[REDACTED]

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5. GENERAL STATISTICAL CONSIDERATIONS

5.1. Reporting Conventions

- Data from all study centers in the main protocol BGB-A317-NSCL-001 and the companion protocol BGB-A317-NSCL-001C will be collected into a single database and analyzed;
- All stratified efficacy analyses will use the stratification factors including age (), chemotherapy regimen (), and region ();
- P-values will be rounded to 4 decimal places. P-values that round to 0.0000 will be presented as '<0.0001' and p-values that round to 1.000 will be presented as '>0.9999';
- Confidence intervals (CIs) will be presented as 2-sided 95% CIs unless specified differently in specific analysis;
- Summary statistics will consist of the number and percentage of subjects (or cycles, if appropriate) in each category for discrete variables, and the sample size, mean, median, Standard Deviation (STDEV), minimum, and maximum for continuous variables;
- All mean and median values will be formatted to one more decimal place than the measured value. Standard deviation values will be formatted to two more decimal places than the measured value;
- All percentages will be rounded to one decimal place. The number and percentage of responses will be presented in the form XX (XX.X%), where the percentage is in the parentheses;
- All listings will be sorted for presentation in order of treatment arm, study center, subject, and date of procedure or event;
- All analysis and summary tables will have the analysis population sample size (ie, number of subjects);
- The day of the first dose of any study drug will be defined as Day 1;
- Baseline value will be defined as the last value on or before the first dose of study drug is administered; if multiple values are present for the same time point, the average of these values will be used as the baseline. For subjects who were not treated, the baseline will be the assessment value taken on the visit of Cycle 1 Day 1 if available; otherwise, the value on or prior to randomization date will be used.

5.2. Analysis Populations

5.2.1. Intent-to-Treat Population/Full Analysis Set

The intent-to-treat (ITT) population includes all randomized subjects regardless of whether the subjects receive any IP or have any efficacy assessment conducted. All efficacy analyses will be based on the ITT population, unless otherwise specified. The efficacy analyses will be performed according to treatment assigned at randomization.

5.2.2. Safety Population

The safety population includes all subjects who receive at least one dose of tislelizumab or placebo. If a subject receives study drug other than the subject's randomized treatment assignment, then the subject is assigned to the treatment arm reflecting the treatment that the subject actually received during the study. All safety analyses will be based on the Safety population, unless otherwise specified.

5.2.3. Per-Protocol Population

The per-protocol (PP) population includes all subjects in the safety population who have met all the eligibility criteria, and have no major protocol violation. The PP population will be used in sensitivity analyses of the primary and key secondary endpoints.

CCI [REDACTED]

5.2.5. HRQoL evaluable Population

The Health-Related Quality of Life (HRQoL) evaluable population will include all subjects included in ITT population who completed the EORTC QLQ-C30 and EORTC QLQ-LC13 assessment at baseline (ie, Cycle 1 Day 1 Visit or Screening Visit if assessment at the Cycle 1 Day 1 Visit was not completed, captured or available) and at least 1 postbaseline assessment visit.

6. SUBJECT DISPOSITION

The total number of subjects screened will be presented, and subjects with screen failure and reasons for screen failure will be summarized by frequency and percentage.

Subject disposition (analysis of population allocation, entered, discontinued, along with primary reason for discontinuation) will be summarized using frequency and percent for treatment period during cCRT, treatment period after cCRT for ITT population.

Reasons for treatment discontinuation will be summarized by treatment arm. The number and percentage of subjects who are in the survival follow-up, lost to survival follow-up, or died at the time of analysis will also be presented.

Reasons for study discontinuation will be summarized for all subjects who discontinue study.

Number of subjects randomized by strata and number of subjects randomized by region, country and site will be summarized. Listings will be provided for subjects who are screened but not enrolled, randomized but not treated, and for discontinued subjects with reason for treatment discontinuation.

7. PROTOCOL DEVIATIONS

The protocol deviations will be identified and assessed by clinical research physician or designee following company standard operational procedure. Protocol deviations and important protocol deviations will be reviewed before database lock to determine the PP population. Events that could trigger exclusion from the PP population include inclusion/exclusion criteria violations, failure to take any study drug as assigned, randomization errors, and prohibited concomitant medications and procedures. In this SAP, important protocol deviation is used interchangeably with major protocol violation.

The important protocol deviations will be summarized separately by treatment arm for the ITT population. A by-subject listing of subjects with important protocol deviations in the ITT population will be provided.



8. DEMOGRAPHICS AND BASELINE CHARACTERISTICS

The demographics and baseline characteristics will be summarized for the ITT population. Individual subject listings will be provided to support the summary tables.

8.1. Demographics

Subject's age (years), height (cm), weight (kg), Body Mass Index (BMI) and Body Surface Area (BSA) at baseline will be summarized descriptively. Sex, race, ethnicity and reproductive status will be summarized by frequency counts.

Age will be calculated as follows: age = Integer of [(Date of informed consent – Date of Birth + 1) / 365.25] or use derived age from eCRF.

BMI will be calculated as follows: BMI (kg/m²) = weight in kg / (height in m)².

BSA will be calculated as follows: BSA (m²) = 0.007184 × (Weight in kg)^{0.425} × (Height in cm)^{0.725}.

8.2. Baseline Characteristics

The following baseline characteristic will be summarized by frequency counts, by treatment arm and overall:

- ECOG performance status at baseline (0, 1, ≥2);
- Disease stage at diagnosis (IIIA, IIIB, IIIC);
- Stage of cancer per blinded independent central review;
- Histology subtype (Adenocarcinoma, Squamous cell carcinoma, Mixed adeno-squamous, Other);
- EGFR mutation (Positive, Negative);
- ALK rearrangement status (Positive, Negative);
- PDL1 result category (Positive, Negative);
- PDL1 scoring cut off (<1, 1 - 24, 25 – 49, ≥ 50, Not Available);
- Pulmonary function results by tests;
- Smoking status (Never, Current, Former).

8.3. Cancer History and Baseline Lesion Status

The following items will be summarized for cancer diagnosis:

- The time from the diagnosis date of the studied disease to first dose date in months, defined as (first dose date – diagnosis date + 1) / 30.4375
- Number of target/non-target lesions overall and by types of lesion;

- Method of assessment for target/non-target lesions
- Sum of target lesion diameters

Subject listings will be provided for all of the above, as well as date of diagnosis.

8.4. Medical History

A summary of medical and surgical history will be presented by MedDRA system and organ class (SOC) and preferred term (PT).

8.5. Prior and Concomitant Therapy

8.5.1. Prior and Concomitant Anti-Cancer Therapy

Prior and concomitant anti-cancer procedures will include radiation therapy for other disease, stem cell transplants and surgeries for any diseases. Prior and concomitant procedures will be tabulated separately.

The number and percentage of subjects who had radiation therapy for other diseases will be presented. For subjects with radiation therapy, the number and percentage of subjects with each type of radiotherapy (External Beam Location, Radio-Immuno Therapy, Brachytherapy, Other) and each site of radiation therapy will be presented.

The number and percentage of subjects who had surgery for any diseases will be presented by study treatment group for overall and by anatomical location.

Prior and concomitant procedures will be listed.

8.6. Prior and Concomitant Medications

Medications reported on the Prior and Concomitant medications eCRF pages will be coded to therapeutic drug classes and generic drug names using the WHO drug dictionary.

8.6.1. Prior Medications

Prior medications are defined as all medications that were started before the first dose of study drug. A summary showing the number and percentage of subjects who took prior medications will be presented by WHO drug dictionary therapeutic drug class and generic drug name. This summary will be presented for the ITT population.

8.6.2. Concomitant Medications

Concomitant medications for the Treatment Period are defined as medications that were initiated before the first dose of study drug and continued during the study treatment, or initiated on/after the date of the first dose of study drug and within 28 days after the date of treatment discontinuation.

Summaries showing the number and percentage of subjects who took concomitant medications will be presented by WHO therapeutic drug class and generic drug name for the ITT population.

9. STUDY TREATMENTS AND EXTENT OF EXPOSURE

Study treatment and extent of exposure summaries will be provided based on the safety population. Descriptive statistics will be provided for treatment duration, number of cycles, cumulative dose, dose intensity, and relative dose intensity by treatment arm. Dose reduction/interruption will also be summarized.

9.1. Treatment Duration

The treatment start date is the date of the first dose of study treatment. For subjects who discontinue early from study treatment, the treatment end date is the date of last dose recorded on the CRF. For subjects who are still on treatment at the time of study closure or clinical cutoff, the treatment end date will be the last treatment dose date or the cutoff date, whichever occurs first.

Treatment duration (in weeks) is calculated as (treatment end date – the date of the first dose of study drug + 1) / 7 and rounded to one decimal place. The treatment durations of a concomitant combination (e.g. tislelizumab + cCRT or placebo + cCRT) and each monotherapy (tislelizumab or placebo), as well as overall treatment duration will be calculated and summarized respectively. Summary statistics for treatment duration (in weeks) as well as a frequency summary of treatment duration categories (<3 weeks, ≥ 3 to < 6 weeks, ≥ 6 to < 9 weeks, ≥ 9 to < 12 weeks, and every 3-week intervals so forth) will be provided.

Descriptive statistics for the total number of treatment cycles subjects received and the number of doses administered for each study drug will be provided. A summary of the frequency of subjects dosed at each cycle will also be provided.

9.2. Cumulative Dose

Cumulative dose will be computed separately for each study drug. Cumulative dose for each study drug is defined as the sum of all actual doses, defined as the values entered on the actual dose administered field on the dosing eCRF, taken across the Treatment Period. Descriptive statistics will be presented for cumulative dose for the safety subjects.

9.3. Dose Intensity

Dose intensity during the treatment is defined as the cumulative dose divided by the treatment duration in weeks. Dose intensity will be calculated separately for each study drug.

Dose intensities will be calculated as follows:

- [REDACTED]
- [REDACTED]
- [REDACTED]

Dose intensity will be presented by each study drug for the Treatment Period of the study for the safety population.

9.4. Relative Dose Intensity

Relative dose intensity by week is the dose intensity divided by the protocol weekly dose, expressed as a percentage. Relative dose intensity will be calculated separately for each study treatment.

- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]

Percentage of protocol dose for each study treatment will be categorized into $<70\%$, $\geq 70\%$ to $<80\%$, and ≥ 80 to $<90\%$ and $\geq 90\%$, and frequency counts will be provided for the safety population.

9.5. Dose Adjustment/Interruption

Dose adjustment for each study drug is defined as when dose administered after Cycle 1 Day 1 is different from the dose the subject receives at the previous dosing visit.

In addition, for each study drug, dose interruption is defined as the dose interruption collected from eCRF.

Treatment exposure and dose adjustment or interruption will be summarized as follows (separately for each study drug):

- Number of cycles and number of doses administered;
- Number and percentage of subjects with at least 1 dose adjustment or interruption, and reasons (Adverse event, Per protocol, investigator decision, or other) for adjustment or reduction;

Number and percentage of subjects with at least one dose adjustment or interruption and number of dose adjustments or interruptions will be presented.

10. EFFICACY ANALYSIS

All efficacy evaluations will be conducted using the ITT population. In addition, the primary and key secondary efficacy endpoints will be analyzed using Per Protocol population. Statistical comparisons will be made between Arm 1 versus Arm 3 or Arm 2 versus Arm 3 stratified by age [REDACTED], chemotherapy regimen [REDACTED], and region [REDACTED]. Efficacy results that will be considered statistically significant after consideration of the strategy for controlling the family-wise Type 1 error rate are described in Section 10.1, Multiplicity. All statistical tests will be one-sided and the corresponding p-values and two-sided confidence intervals (CIs) for intended point estimates will be reported.

10.1. Multiplicity

There are 2 primary hypotheses in this study:

- H_1 : PFS in Arm 1 \leq Arm 3 versus PFS in Arm 1 $>$ Arm 3
- H_2 : PFS in Arm 2 \leq Arm 3 versus PFS in Arm 2 $>$ Arm 3

CCI [REDACTED]

There will be one interim and one final analysis for PFS, and one interim and one final analysis for OS, respectively. The interim OS analysis will occur at the same as the final PFS analysis. Therefore, there will be 3 data cutoff time points in this study:

Although PFS is the primary endpoint of this study and the final PFS analysis will be completed at the second data cutoff time point, the study may continue to follow up for overall survival until a prespecified total number of OS events accumulates, if either of the PFS hypotheses are rejected at the interim or the final PFS analysis.

A group sequential design is implemented based on Lan-Demets spending function that approximates the O'Brien-Fleming boundary for each of the primary hypotheses for the PFS endpoint. The hypotheses associated with the key secondary endpoint OS:

- H_3 : OS in Arm 1 \leq Arm 3 versus OS in Arm 1 $>$ Arm 3

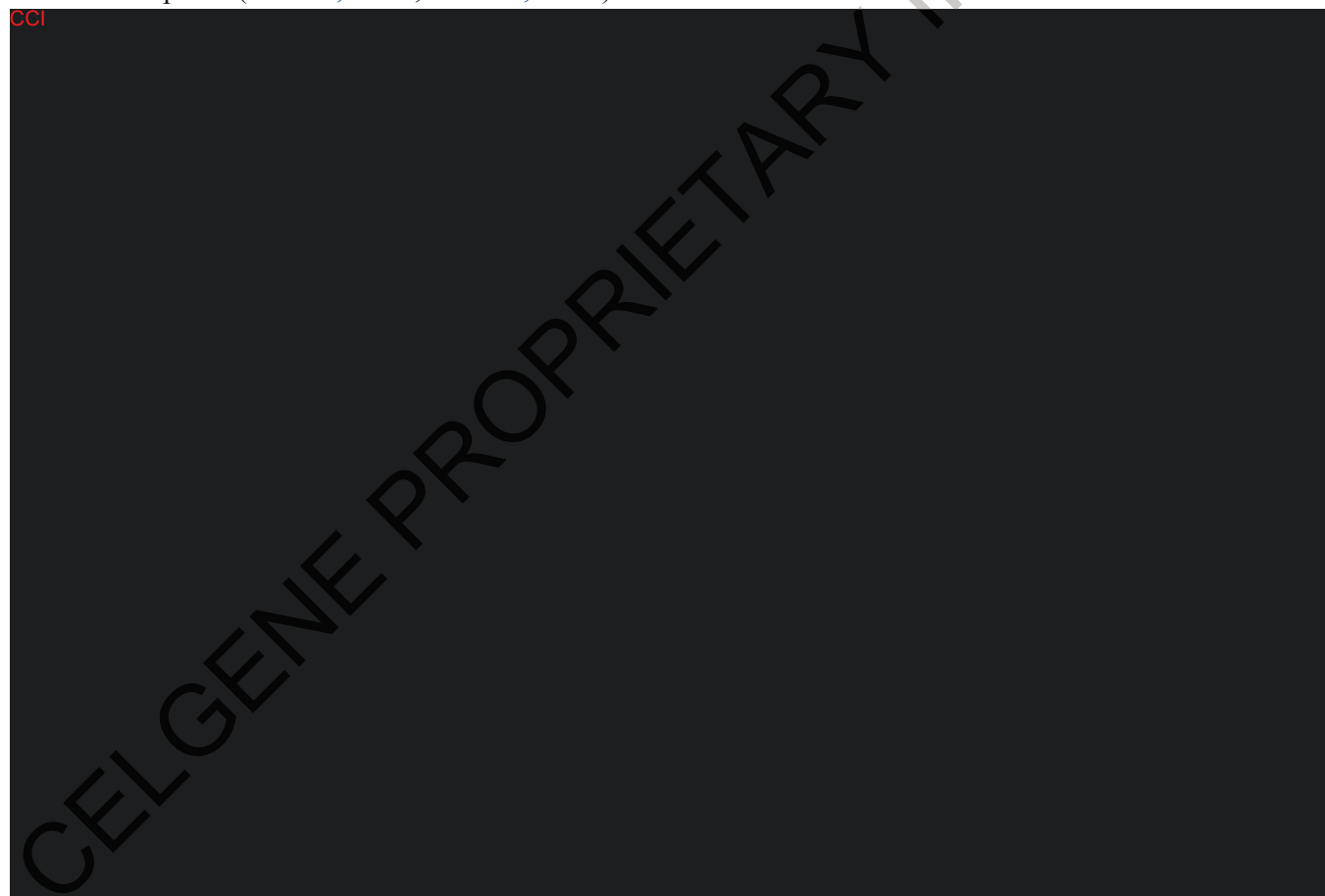
- H_4 : OS in Arm 2 \leq Arm 3 versus OS in Arm 2 $>$ Arm 3

will be tested only if either one of the primary hypotheses for PFS is rejected at the interim or the final PFS analysis. In addition, the other 2 key secondary endpoints, OS at 24 months (OS 24) and ORR, will also be tested if both the PFS and OS hypotheses in the same pairwise comparison of treatment groups are rejected. The hypotheses associated with OS 24 and ORR are:

- H_5 : OS 24 in Arm 1 \leq Arm 3 versus OS 24 in Arm 1 $>$ Arm 3
- H_6 : OS 24 in Arm 2 \leq Arm 3 versus OS 24 in Arm 2 $>$ Arm 3
- H_7 : ORR in Arm 1 \leq Arm 3 versus ORR in Arm 1 $>$ Arm 3
- H_8 : ORR in Arm 2 \leq Arm 3 versus ORR in Arm 2 $>$ Arm 3

The overall type one error rate control strategy here follows the graphic approach as described by Maurer and Bretz (Maurer, 2013), and can be depicted by the following graph. The local alpha will be dynamically determined by the given spending function of the group sequential design for each endpoint (Glimm, 2010; Maurer, 2013).

CCI



The alpha propagation strategy here allows passing alpha from one hypothesis to the other, provided that the hypothesis is rejected at the interim or final analysis. Therefore, depending on rejection or acceptance of other hypotheses, the significance level for testing each of the

hypotheses may be updated from the initially allocated alpha. Additionally, to control the type one error due to multiple looks of OS data at the interim and the final OS analysis, a group sequential design based on an alpha spending function that approximates the O'Brien-Fleming boundary will also be implemented for either one of the OS hypotheses. The actual boundaries will depend on the number of OS events, or information time, at the time of final PFS analysis. Similar alpha control approach will be implemented for the other key secondary endpoints OS 24 and ORR. Notably, if one or more hypotheses are rejected at the interim or final analysis, the superiority boundaries for the remaining unrejected hypotheses will be updated based on the alpha propagation strategy as described by Maurer and Bretz ([Maurer, 2013](#)) using the graph above.

The family-wise type one error rate will be CCI for the primary endpoint, PFS, and 3 key secondary endpoints, OS, OS 24 and ORR, for the comparisons of Arm 1 vs Arm 3 and Arm 2 vs Arm 3.

If both pairwise comparisons of Arm 1 and Arm 2 are statistically significantly better than Arm 3 for PFS or OS or OS 24 or ORR, comparison between Arm 1 and Arm 2 with estimates of hazard ratio or difference in rate and corresponding 95% CIs, will be provided as a supportive analysis.

10.2. Analysis of Primary Efficacy Endpoint

The primary efficacy endpoint, PFS will be analyzed using the ITT and the PP Populations. The PFS is defined as the time in months from the date of randomization to the date of disease progression according to RECIST 1.1 criteria (documented by CT-scan result, not including symptomatic deterioration) or death (any cause) on or prior to the clinical cutoff date, whichever occurs earlier.

$$\text{PFS} = (\text{Date of Disease Progression or Death} - \text{Date of Randomization} + 1) / 30.4375$$

Subjects who do not have disease progression or have not died as of the data cutoff date will be censored at the time of the last radiologic assessment where the subject was documented to be progression-free prior to the data cutoff date. In the event that a new anti-cancer therapy is initiated for a subject prior to documented progression (or death), the subject will be censored at the time of the last radiologic assessment where the subject was documented to be progression-free prior to the new anti-cancer therapy. Subjects with a single missing radiologic assessment prior to a visit with documented disease progression (or death) will be analyzed as a PFS event at the time of the radiologic assessment that shows progression or death (whichever is earlier). Subjects with two or more consecutive missing radiologic assessments prior to a visit with documented disease progression (or death) will be censored at the time of the last radiologic assessment where the subject was documented to be progression-free prior to the first of the two or more consecutive missing visits. The PFS censoring rule is further illustrated in [Table 2](#).

The distribution of PFS will be estimated using the Kaplan-Meier method. The comparison of PFS between treatment arms (Arm 1 versus Arm 3 or Arm 2 versus Arm 3) will be conducted using a stratified log-rank test with age CCI, chemotherapy regimen (CCI), and region (CCI) as stratification factors. The hazard ratio (between Arm 1 versus Arm 3 or Arm 2 versus Arm 3) and the corresponding 95% confidence interval will also be provided based on a stratified Cox

proportional hazard model. The median PFS (with 95% confidence interval) and estimation of PFS rate (with 95% confidence intervals) for specific time points (eg, 3 months, 6 months etc.) will be provided for each treatment arm. The median differences with 95% CIs between each of a pair compared arms will be calculated using Kosorok’s method ([Kosorok, 1999](#)).

If both pairwise comparisons of Arm 1 and Arm 2 are statistically significantly better than Arm 3 for PFS, comparison between Arm 1 and Arm 2 with estimate of hazard ratio and corresponding 95% CI, will be provided as a supportive analysis.

Table 2: Censoring Rules for PFS

Value of Progression-free Survival Date (ADT)	Censored (Y,N)	Derivation
ADT = min(death date, progression date)	N	If a subject died or had disease progression, and the time interval between the death date/progression date and the previous tumor assessment date with progression-free response or the randomization date is less than or equal to two scheduled tumor assessment visits (91 days in the first 36 weeks and 133 days after 36 weeks from the first study dose).
ADT = the last progression-free assessment date/ randomization date	Y	If a subject died or had disease progression, and the time interval between the death date/progression date and the previous tumor assessment date with progression-free response or the randomization date is greater than two scheduled tumor assessment visits (91 days in the first 36 weeks and 133 days after 36 weeks from the first study dose).
ADT = the last tumor assessment date/randomization date	Y	If a subject did not die or have progression, and did not receive any subsequent anticancer chemotherapy. If there was no post-baseline tumor assessment, then ADT = the randomization date.
ADT = the last tumor assessment date on or prior to start of subsequent anticancer therapy/randomization date	Y	If a subject did not die or have progression on or prior to start of subsequent anticancer therapy, or a subject died/progressed after the start of sequent anticancer therapy. If there was no post-baseline tumor assessment, then ADT = the randomization date.
ADT = analysis date; N = no; Y = yes. Note: Progression-free response refers to a response that was neither progressive disease (PD) nor not-evaluable (UE).		

10.3. Analyses of Secondary Efficacy Endpoints

The secondary efficacy endpoints will be analyzed based on ITT population. For the key secondary efficacy endpoints of OS, OS at 24 months and ORR, these will be analyzed using the ITT and the PP population respectively. Statistical analyses of Patient-Reported Outcomes relevant secondary endpoints will be described in Section 12 of this document.

10.3.1. Overall Survival

The key secondary endpoint of OS is defined as the time from randomization to death due to any cause. Subjects without documented death at the time of analysis will be censored at the last-known-to-be-alive date. OS is defined as the duration (in months) between randomization and death from any cause:

$$OS = (\text{Date of Death} - \text{Date of Randomization} + 1) / 30.4375$$

Subjects who are still alive at the end of the study or clinical data cut will be censored at the last-known-to-be-alive date or clinical cutoff date, whichever is earlier.

The distribution of OS will be estimated using Kaplan-Meier method. A stratified log-rank test will be used to compare treatment groups in OS. The median OS (with 95% confidence interval) and estimation of OS rate (with 95% confidence intervals) for different timepoints will be provided by treatment arm. The median differences with 95% CIs between each of a pair compared arms will be calculated using Kosorok's method ([Kosorok, 1999](#)). The hazard ratio (between Arm 1 or Arm 2 versus Arm 3) and the corresponding 95% confidence interval will also be provided based on a stratified Cox regression model.

If both pairwise comparisons of Arm 1 and Arm 2 are statistically significantly better than Arm 3 for OS, comparison between Arm 1 and Arm 2 with estimate of hazard ratio and corresponding 95% CI, will be provided as a supportive analysis.

10.3.2. OS at 24 Months

The key secondary endpoint OS at 24 months is defined as the proportion of subjects alive at 24 months (OS 24).

The point estimate and the corresponding 95% confidence interval for each treatment arm will be estimated using Kaplan-Meier method.

The treatment comparisons for OS 24 will be performed using the cloglog transform approach as described in [Klein, 2007](#). The p-value of equality of the survival functions will be provided using this approach.

If both pairwise comparisons of Arm 1 and Arm 2 are statistically significantly better than Arm 3 for OS 24, comparison between Arm 1 and Arm 2 with estimate of OS 24 difference and corresponding 95% CI, will be provided as a supportive analysis.

10.3.3. Objective Response Rate

The key secondary endpoint of ORR is defined as the percentage of subjects who achieve a CR or PR based on the independent reviewer assessment using RECIST v1.1 criteria. The number and percentage of those with a tumor response of partial response (PR), or complete response

(CR) will be presented, as well as the number and percentage with each of progressive disease (PD), SD, PR, CR, and Not-evaluable (NE).

The ORR for each treatment arm will be summarized using 95% Clopper-Pearson confidence interval. The difference in ORR between treatment arms and the associated 95% confidence interval will be estimated using stratified Wilson score method. A Cochran-Mantel-Haenszel (CMH) test will be used to compare ORR between treatment arms.

If both pairwise comparisons of Arm 1 and Arm 2 are statistically significantly better than Arm 3 for ORR, comparison between Arm 1 and Arm 2 with estimate of ORR difference and corresponding 95% CI, will be provided as a supportive analysis.

10.3.4. Duration of Response

The DOR is defined as the time from the first tumor assessment when the CR/PR response criterion is first met to the date of disease progression based on independent reviewers' assessment following RECIST v1.1 criteria or death, whichever is earlier.

For subjects who had a confirmed CR or PR, the duration of overall response is measured from the time measurement criteria are first met for CR/PR (whichever is first recorded) until the first date that progressive disease is radiologically documented (taking as reference for progressive disease the smallest measurements recorded on study) or death.

Subjects who are non-responders (i.e., do not achieve at least a PR) will be excluded from this analysis.

The duration of response will be analyzed using similar methods as described for the analysis of PFS.

10.3.5. Alive and Progression-Free at 12 or 18 Months

The proportion of subjects alive and progression free at 12 months (APF12) or 18 months (APF18) will be summarized. The point estimate and the corresponding 95% confidence interval for each treatment arm will be estimated using Kaplan-Meier method.

Treatment comparisons for APF12 and APF18 will be based on the cloglog transform approach as described in [Klein, 2007](#). The p-value of equality of the survival functions will be provided using this approach.

10.3.6. Time to Distant Metastasis

TTDM will be defined as the time from the date of randomization until the first date of distant metastasis or death in the absence of distant metastasis. Distant metastasis is defined as any new lesion that is outside of the radiation field according to RECIST v1.1 or proven by biopsy.

Subjects who do not have documented new distant lesion or have not died as of the data cutoff date will be censored at the time of the last radiologic assessment or biopsy where the subject was documented to be distant lesion free prior to the data cutoff date.

Time to distant metastasis will be analyzed using similar methods as described for the analysis of PFS.

10.3.7. Proportion of subjects who continue to monotherapy phase

The proportion of subjects who received at least one dose of tislelizumab or placebo in the monotherapy phase before progression based on blinded independent reviewer assessment following RECIST v1.1 criteria, will be compared for Arm 1 versus Arm 2 and 3 combined. The proportion will be summarized using point estimate and 95% Clopper-Pearson confidence interval for Arm 1 versus Arm 2 and 3. The difference between treatment arms and the associated 95% Wilson score confidence interval will be provided. A Cochran-Mantel-Haenszel (CMH) test will be used to compare the proportion.

In addition, the proportion of subjects who are progression free at the end of cCRT will be compared for Arm 1 versus Arm 2 and 3 combined. Progression free at the end of cCRT is defined as CR or PR or SD based on blinded independent reviewer assessment following RECIST v1.1 criteria at week 6.

10.4. Subgroup Analysis

The primary and key secondary efficacy endpoints will also be analyzed within the following subgroups, note that the age, chemotherapy regimen^{CCI} [REDACTED] region (CCI [REDACTED]), baseline ECOG will be based on the clinical data instead of randomization data:

1. [REDACTED]
1. Age [REDACTED]);
2. ECOG PS (0 vs 1);
3. Sex (male vs female);
4. Stage at diagnosis (Stage IIIA vs Stage IIIB vs Stage IIIC);
5. Chemotherapy regimen^{CCI} [REDACTED]);
6. Mutation (EGFR mutation or ALK rearrangement vs EFGR and ALK Wild-Type);
7. PD-L1 (positive (TPS \geq 1%) vs negative (TPS < 1%));
8. Smoking status (never vs current vs former);
9. Histology subtype (adenocarcinoma vs squamous cell carcinoma vs mixed adeno-squamous vs other).

A forest plot will be provided based on the HRs or differences in rate for each subgroup.

The consistency of the treatment effect will be assessed in the context of the primary efficacy analysis model with terms for treatment, stratum, its interaction with treatment, and the covariate. Treatment effects and nominal 95% confidence intervals by category for the classification variables listed above will be provided. Formal statistical testing of these interactions will not be performed.

11. SAFETY ANALYSIS

The purpose of this section is to describe the safety analyses for the Treatment Period of the study. Adverse events and laboratory values will be analyzed based on the safety population, per treatment arm and for treatment-related TEAEs or TEAEs with action taken, also by specific drug.

11.1. Adverse Events

Adverse events will be analyzed in terms of treatment-emergent adverse events (TEAEs) which are defined as any adverse events that had an onset date or a worsening in severity from baseline on or after the first dose of study drug up to 30 days following study drug discontinuation or initiation of new anticancer therapy, whichever occurs first. TEAEs also include all immune-related AEs recorded up to 90 days after the last dose of tislelizumab or placebo, regardless of whether or not the subject starts a new anticancer therapy. In addition, any serious AE with an onset date more than 30 days after the last dose of study drug that is assessed by the investigator as related to study drug will be considered a TEAE. All AEs will be coded using the Medical Dictionary for Regulatory Affairs® (MedDRA).

Treatment-related TEAE will be summarized for each treatment arm. If a subject experiences multiple occurrences of the same AE with different relationship to study medication categories, the subject will be counted once, as a relationship category of treatment-related. TEAEs with a missing relationship will be presented in the summary table as a relationship category of “treatment-related”.

The incidence of TEAEs will be summarized for each treatment arm by MedDRA SOC and PT in a descending order of frequency of SOC and PT within each SOC based on the combination arm. If a subject experiences multiple AEs under the same SOC or PT, then the subject will be counted only once for that SOC or PT.

The toxicity of AEs will be graded 1 to 5 according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. For all other AEs not described in the CTCAE criteria, the toxicity will be assessed by the investigator as mild (grade 1), moderate (grade 2), severe (grade 3), life-threatening (grade 4) or death (grade 5). If a subject experiences the same AE more than once with different toxicity grade, then the event with the highest grade will be tabulated in “by grade” tables. If a subject experiences multiple AEs under the same preferred term (system organ class), then the subject will be counted only once for that preferred term (system organ class). In addition, AEs with a missing intensity will be presented in the summary table as an intensity category of “Missing.”

Deaths during the study will be summarized by cause categories. AEs regarded as primary cause of deaths, as reported on CRF, will also be summarized by SOC and PT. For both types of summaries, on-treatment (within 30 days after the last dose of study treatment) and post-treatment deaths will be summarized separately.

Tables summarizing the incidence of TEAEs will be generated for each of the following:

- All TEAEs;

- TEAEs reported as treatment-related;
- Serious TEAEs;
- Treatment-related serious TEAEs;
- All TEAEs with grade 3-4;
- Treatment-related grade 3-4 TEAEs;
- TEAEs leading to death;
- Treatment-related TEAEs leading to death;
- TEAEs leading to drug discontinuation;
- All TEAEs by CTCAE grade as well as grade 1-2 vs. grade 3-4;
- All death within 30 days of last dose with cause of death.

Listings for the corresponding summary tables will be presented separately. Non-treatment-emergent AEs will also be listed.

11.2. Immune-related Adverse Events

The treatment-emergent immune-related adverse event (TEirAE) will be summarized by treatment arm:

- Thyroid Disorders
- Hypophysitis
- Pneumonitis
- Neurological Toxicity
- Colitis
- Eye Disorders
- Hepatitis
- Renal Toxicity
- Dermatology
- Joint or muscle inflammation
- Myocarditis

11.3. Clinical Laboratory Evaluations

Clinical laboratory values from the central laboratories will be graded according to NCI CTCAE version 5.0 for applicable tests. The worst grade during the treatment period will be summarized by treatment arm. Frequency distributions for shift from baseline to the worst grade during treatment period will be presented by treatment arm. Normal ranges will be used to determine the categories of High, Low, and Normal for lab tests that have no severity grade.

Listings of clinical laboratory data from central laboratory with abnormal flags will be provided by subjects and tests. Listings will also be provided for the local laboratory data.

11.3.1. Hematology

Hemoglobin, hematocrit, red blood cell count and morphology, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, white blood cell count with absolute and differential and percent (neutrophils, lymphocytes, monocytes, eosinophils, basophils, and bands), platelet count, reticulocytes, erythrocyte sedimentation rate, international normalized ratio, prothrombin time, partial thromboplastin time will be collected in hematology panel. Additional laboratory samples may be collected as clinically indicated.

In order to investigate the maximal degree of myelosuppression, the NCI CTCAE grade for hemoglobin, leukocytes, lymphocytes, neutrophils and platelets will be summarized by the worst grade in each treatment cycle and by the worst grade overall (i.e., any time after first dose of study drug). The number and percentage of subjects with each NCI CTCAE grade will be presented. A shift table representing the shift from the baseline grade to the worst grade will be provided for each of these laboratory tests.

Treatment group differences in each laboratory parameter with respect to the NCI CTCAE grades will be summarized by the frequency distribution of subjects with the grades.

All laboratory parameters will be summarized by descriptive statistics within each treatment arm, as appropriate.

11.3.2. Clinical Chemistry

Serum chemistry panel includes sodium, potassium, bicarbonate, calcium, magnesium, phosphorus, blood urea nitrogen, serum creatinine and clearance, uric acid, glucose, lactic dehydrogenase (LDH), total protein, albumin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, gamma glutamyl transferase, total, direct and indirect bilirubin, fibrinogen, ferritin. Additional laboratory samples may be collected as clinically indicated.

Hepatic and renal function will be summarized using the NCI CTCAE grade for ALT (SGPT), AST (SGOT), albumin, total bilirubin, creatinine, potassium, and sodium. The number and percentage of subjects that have each NCI CTCAE grade will be summarized using the worst grade for each cycle and overall. A shift table representing the shift from the baseline grade to the worst grade will be provided for each of these laboratory tests.

Treatment group differences in each laboratory parameter with respect to the NCI CTCAE grades will be summarized by the frequency distribution of subjects with the grades.

All laboratory parameters will be summarized by descriptive statistics within each treatment arm, as appropriate.

11.4. Vital Sign Measurements

Vital signs (Weight, Temperature, Systolic and Diastolic Blood Pressure, Pulse and Respiratory rate) will be recorded at screening and on Day 1 of each cycle and EOT. Vital sign data will be listed.

11.5. Physical Examination

Physical Examination will be recorded in source documentation (i.e. not collected on CRF) only and hence no table and listings will be produced.

11.6. Electrocardiograms

Triplicate 12-lead ECGs will be recorded at screening and EOT and will be assessed locally. The 12-lead ECGs (12-lead at 25 mm/sec reporting rhythm, ventricular rate, PR-interval, QRS complex, QT interval, and QTc interval) will be performed after the subject has been in the supine position for at least 5 minutes. Shift from baseline to most abnormal post-baseline qualitative assessment of ECG abnormality (i.e., 'Normal', 'Abnormal, not clinically significant', and 'Abnormal, clinically significant') will be displayed in cross-tabulations by treatment.

11.7. ECOG Performance Status

The Eastern Cooperative Oncology Group (ECOG) score runs from 0 to 5, with 0 denoting perfect health and 5 denoting death. ECOG performance status (PS) scores will be assessed and reported on the appropriate eCRF at screening, Day 1 of each cycle and at EOT. A shift table representing the shift from the baseline to the worst post-baseline ECOG PS scores will be provided for each treatment cycle and overall.

11.8. Ophthalmic Examinations

The analysis of data from ophthalmic exams is under discussion; details will be provided in a subsequent SAP version.

11.9. Pregnancy test

A by-subject listing of pregnancy test and results will be provided for all female subjects of childbearing potential.

The purpose of this section is to define the safety parameters for the study. All summaries of safety data will be conducted using the safety population.

12. QUALITY OF LIFE ANALYSIS

The predominant patient-reported lung cancer symptoms (appetite loss, cough, hemoptysis, chest pain, dyspnea, and fatigue) assessed by the EORTC QLQ-C30 and its lung cancer module LC13 will be a predefined secondary endpoint; CCI

12.1. EORTC QLQ-C30 and LC13

Patient reported outcome validated instruments (EORTC QLQ-C30 with the lung module LC13) will be used to assess the selected lung cancer symptoms: appetite loss, cough, hemoptysis, chest pain, dyspnea, and fatigue, as secondary efficacy endpoints. CCI

The EORTC QLQ-C30 and LC-13 scores will be calculated according to scoring algorithms defined by the authors. Missing response items will not be imputed. A domain with multiple items will be scored when 50% or more items in the domain have non-missing responses. Scores are transformed to a 0 to 100 scale, higher scores indicating better QoL, better functioning, or more severe symptoms.

To assess the extent of missing data at each assessment visit by treatment group, the PRO compliance rates for the EORTC QLQ-C30 and LC-13 will be estimated per treatment group on the ITT population. Subjects are considered compliant with completion of the EORTC QLQ-C30 and LC-13 assessment if at least half of the items are non-missing at a given assessment visit.

To assess the effect of study treatments on HRQoL, the following analyses will be conducted for the selected symptoms identified as secondary efficacy endpoints based on the HRQoL evaluable population.

Baseline scores, post-baseline scores and change from baseline will be statistically described for all domains and symptoms (as applicable) by treatment arm. To interpret the difference in change score from baseline between treatment groups and change score at the individual level, values for clinically-meaningful change in EORTC QLQ-C30 domain scores reported in EORTC scoring manual ([Osoba, 1998](#)) will be considered. Other values defined according to cut-off values for clinically-meaningful change across different domains published by Cocks et al ([Cocks, 2012](#)) will also be considered for sensitivity analysis.

Count and percent of subjects with improvement and worsening in scores from their baseline score will be summarized by treatment group over study visit. Improvement and worsening will be defined based on values considered for clinically-meaningful change from baseline ([Osoba,](#)

1998; Cocks, 2012). Time to the first minimal clinically important improvement in scores will be examined using Kaplan-Meier method.

Analysis for the following will be provided in a separate HRQoL statistical analysis plan. The HRQoL statistical analysis plan will be appended to the specific HRQoL report.

Descriptive statistics of the baseline HRQoL domain scores and key demographic and disease characteristics will be summarized by treatment group and overall for the HRQoL-evaluable and non-evaluable populations. The comparability of the HRQoL-evaluable and non-evaluable populations will be assessed to mitigate the potential selection bias.

The relationship between selected clinical efficacy responses (PFS, OS, ORR) and selected symptoms defined as secondary endpoints will also be explored.

CCI [REDACTED]

CCI [REDACTED]

[REDACTED]

[REDACTED]

CCI [REDACTED]

[REDACTED]

CCI [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

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CCI

[REDACTED]

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CELGENE PROPRIETARY INFORMATION

15. INTERIM ANALYSIS

15.1. General Information

An independent Data Monitoring Committee will be established and will include medical oncologists and a statistician, all of whom are not otherwise involved in the study conduct. During the course of the study, the DMC will review the safety data regularly. The DMC will offer recommendations based on periodic evaluations of comparative safety data, in accordance with criteria outlined in the DMC Charter. An independent statistician will prepare the reports to the DMC members for each scheduled meeting. Details will be provided in the DMC charter.

[REDACTED]

may continue during these IDMC safety reviews.

Full details of the IDMC procedures and processes can be found in the IDMC Charter.

15.2. Statistical Approaches for Control of Alpha

One interim analysis for PFS and one interim analysis for OS are planned for this study.

[REDACTED]

The approximate timeline for interim and final analyses, along with the superiority boundaries for the pairwise treatment comparison in PFS ^{CCI}

[REDACTED] updated according to the actual number of events observed in the 2 treatment groups in the pairwise comparison, and the significance level updated due to rejection of other hypotheses as described in the protocol. Celgene anticipates accrual will be completed before an interim analysis of PFS is performed and the study is planned to continue until completion of the final PFS and OS analyses.

Table 3: CCI [REDACTED]

[REDACTED]				
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]				
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

16. CHANGES TO THE STATISTICAL ANALYSES SECTION OF THE PROTOCOL

Per BeiGene press release excerpt from 17 June 2019:

BeiGene, Ltd. (NASDAQ: BGNE; HKEX: 06160), a commercial-stage biopharmaceutical company focused on developing and commercializing innovative molecularly-targeted and immuno-oncology drugs for the treatment of cancer, today announced that it has entered into a mutual agreement with Celgene Corporation to terminate the parties' global collaboration for tislelizumab, BeiGene's investigational anti-PD-1 antibody.

Tislelizumab is the investigational agent in the BGB-A317-NSCL-001 (RATIONALE 001) study, which is being conducted in collaboration with BeiGene. For the reasons noted above, Celgene is closing the BGB-A317-NSCL-001 (RATIONALE 001) study.

Subject PPD is the only subject randomized and treated in BGB-A317-NSCL-001. Since the study is being closed no other subjects will be randomized or treated. The study treatment was unblinded at investigator request and the subject was randomized to treatment arm 2 (i.e. placebo+CRT for 2 cycles followed by tislelizumab monotherapy) and had received only one dose of placebo.

In this SAP the following subgroup analyses were added: Smoking status (never vs current vs former), Stage at diagnosis (Stage IIIA vs Stage IIIB vs Stage IIIC), Histology subtype (adenocarcinoma vs squamous cell carcinoma vs mixed adeno-squamous vs other). In Protocol Section 9 the above subgroup analyses are not described. These subgroup analyses will not be performed as result of the study closure.

The decision of closing the study in very early stage is leading to the decision not to conduct any planned statistical analysis. As a consequence, the SAP is remaining in this stable draft version.

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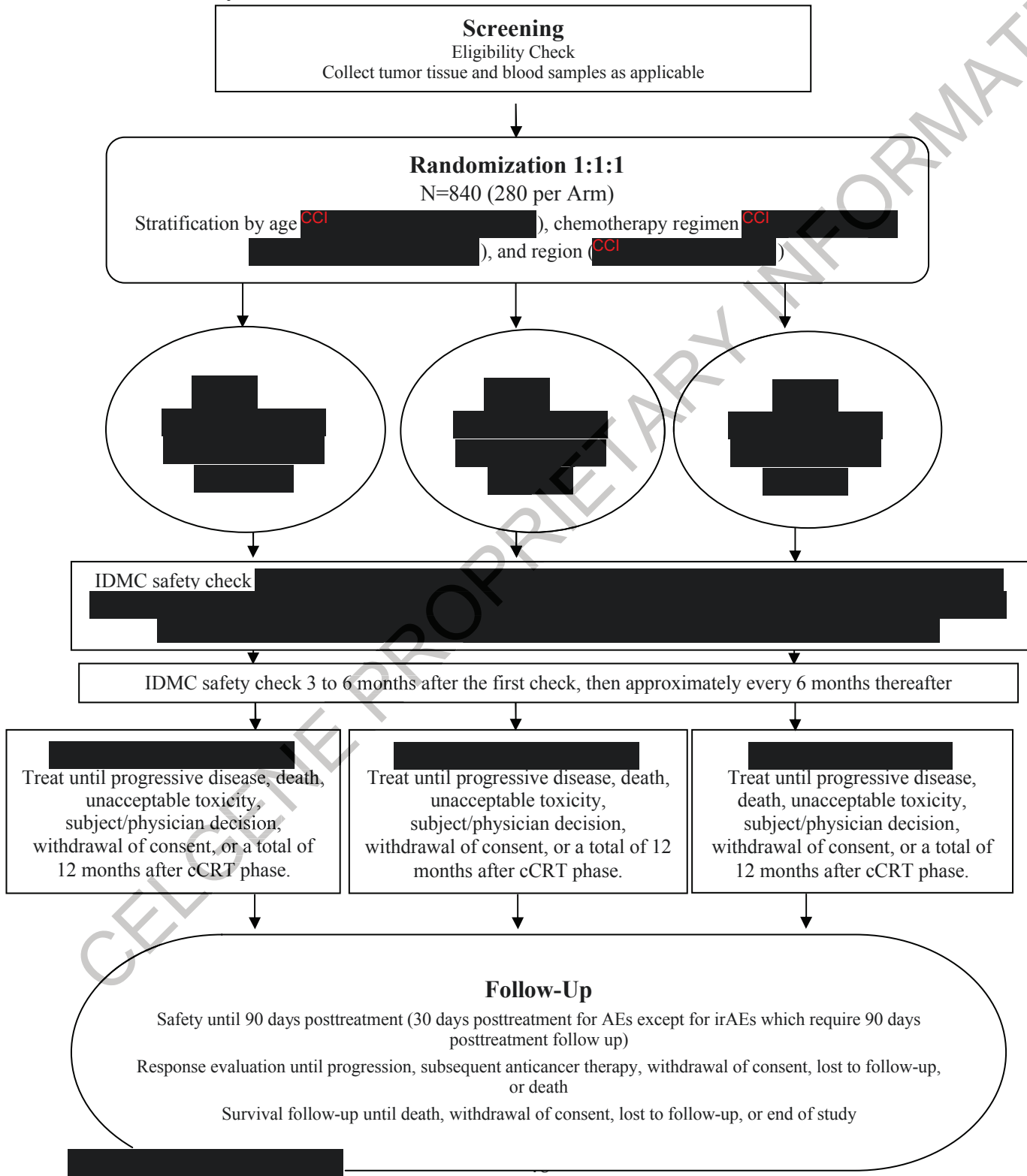
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18. APPENDICES

18.1. Study Schematic and Study Events

18.1.1. Study Schematic



Abbreviations: C1D1 = Cycle 1 Day 1; cCRT = concurrent chemoradiotherapy; IDMC = independent data monitoring committee; [redacted]; [redacted]

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18.1.2. Table of Study Events

Events	Screening ^a	Treatment Period During cCRT						Treatment Period After cCRT Up to 12 Months of Treatment				Follow-up Period			
	Day -28 to -1	D1 ^b	D8	D15	D22	D29	D36	D43	D50	D57	Day 1 of each 21- Day Cycle (starting D64)	EOT ^c	30-Day FU	90-Day FU ^d	PD/ Survival
Window (days)	-	+3	±3	±3	±3	±3	±3	±3	±3	±3	±3		±7	±7	±14
STUDY ENTRY AND GENERAL ASSESSMENTS															
Informed consent	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Inclusion/exclusion criteria	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-
IRT registration	X	X	-	-	X	-	-	X	-	-	X	X	-	-	-
Complete medical history	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Demographics	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Disease history	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Prior/concomitant medication evaluation	Continuous from ≤ 28 days prior to randomization until 30 days post last dose of study treatment												-	-	
Prior/concomitant procedures evaluation	Continuous from ≤ 28 days prior to randomization until 30 days post last dose of study treatment												-	-	
EGFR/ALK testing on tumor tissue (if status not available)	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-

(Continued)

Events	Screening ^a	Treatment Period During cCRT						Treatment Period After cCRT Up to 12 Months of Treatment				Follow-up Period				
	Day -28 to -1	D1 ^b	D8	D15	D22	D29	D36	D43	D50	D57	Day 1 of each 21- Day Cycle (starting D64)	EOT ^c	30-Day FU	90-Day FU ^d	PD/ Survival	
Window (days)	-	+3	±3	±3	±3	±3	±3	±3	±3	±3	±3		±7	±7	±14	
Confirmation of mediastinal nodal involvement, if applicable (the protocol Section 4.2)	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Patient Reported Outcomes: EORTC QLQ-C30, LC13	X	X	-	-	X	-	-	X	-	-	X	X	X	-	-	
SAFETY ASSESSMENTS																
Adverse event evaluation ^e	Continuous from informed consent until 30 days post last dose of study treatment for AEs; 90 days post last dose of tislelizumab/placebo for irAEs														-	
Physical examination	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-	
Vital signs/weight ^f	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-	
Performance status ECOG	X	X	-	-	X	-	-	X	-	-	X	X	X	-	-	
Height	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Body surface area calculation	-	X	X	X	X	X	X	-	-	-	-	-	-	-	-	
Pulmonary function test	X	Only if clinically indicated										-	-	-	-	
12-lead electrocardiogram	X	X	Only if clinically indicated										X	X	-	-

(Continued)

Events	Screening ^a	Treatment Period During cCRT						Treatment Period After cCRT Up to 12 Months of Treatment				Follow-up Period				
	Day -28 to -1	D1 ^b	D8	D15	D22	D29	D36	D43	D50	D57	Day 1 of each 21- Day Cycle (starting D64)	EOT ^c	30-Day FU	90-Day FU ^d	PD/ Survival	
Window (days)	-	+3	±3	±3	±3	±3	±3	±3	±3	±3	±3		±7	±7	±14	
Left ventricular ejection fraction	X	Only if clinically indicated											-	-		
OCT (or equivalent diagnostic test) and visual acuity tests ^e	X	Approximately every 15 weeks (± 7 days) during study treatment										X ^g				
Hematology laboratory ^{fh}	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-	-
Chemistry laboratory ^{fh}	X	X	X	X	X	X	X	X	X	X	X	X	X	X	-	-
Coagulation laboratory (PT, PTT, INR) ^h	X	X	-	-	X	-	-	X	-	-	X	X	X	X	-	-
Thyroid function ^h	X	X	-	-	X	-	-	X	-	-	X	X	X	X	-	-
C-reactive protein	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HBV/ HCV test ⁱ	X	If clinically indicated. For subjects who have detectable HBV DNA or HCV RNA at screening or upon repeat testing, respective viral load test every 4 cycles (ie, Day 1 of Cycles 5, 9, 13, etc.).											-	-		
Urinalysis	X	If clinically indicated											-	-		
Serum β-hCG pregnancy test	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Urine β-hCG pregnancy test ⁱ	X	X	-	-	X	-	-	X	-	-	X	X	X	X	-	-

(Continued)

Events	Screening ^a	Treatment Period During cCRT						Treatment Period After cCRT Up to 12 Months of Treatment				Follow-up Period			
	Day -28 to -1	D1 ^b	D8	D15	D22	D29	D36	D43	D50	D57	Day 1 of each 21- Day Cycle (starting D64)	EOT ^c	30-Day FU	90-Day FU ^d	PD/ Survival
Window (days)	-	+3	±3	±3	±3	±3	±3	±3	±3	±3	±3		±7	±7	±14
EFFICACY ASSESSMENTS															
Tumor assessment CT/MRI	X	Every 6 weeks after randomization for the first 36 weeks (± 7 Days), and every 9 weeks from Week 36 (± 7 Days) onward until disease progression, start of a new anticancer therapy, or withdrawal of consent from the entire study													
FDG-PET/CT	X	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CT scan, with contrast, of the head or brain MRI with contrast	X	Only if clinically indicated													
CCI															

(Continued)

Events	Screening ^a	Treatment Period During cCRT						Treatment Period After cCRT Up to 12 Months of Treatment				Follow-up Period			
	Day -28 to -1	D1 ^b	D8	D15	D22	D29	D36	D43	D50	D57	Day 1 of each 21-Day Cycle (starting D64)	EOT ^c	30-Day FU	90-Day FU ^d	PD/Survival
Window (days)	-	+3	±3	±3	±3	±3	±3	±3	±3	±3	±3		±7	±7	±14
CCI [REDACTED]	█	█	█	█	█	█	█	█	█	█	█ progression				
TREATMENT															
CCI [REDACTED]															
Administer IP: tislelizumab/placebo	-	X	-	-	X	-	-	X ^e	-	-	X	-	-	-	-
CCI [REDACTED]															
Administer radiotherapy ^g	-	60 Gy in 30 fractions (2 Gy per day/5 days per week)						-	-	-	-	-	-	-	-
Accountability tislelizumab/placebo	-	X	-	-	X	-	-	X	-	-	X	-	-	-	-
Accountability etoposide/cisplatin	-	X	X			X	X	-	-	-	-	-	-	-	
CCI [REDACTED]															
Administer IP: tislelizumab/placebo	-	X			X			X			X ^e				

(Continued)

Events	Screening ^a	Treatment Period During cCRT						Treatment Period After cCRT Up to 12 Months of Treatment				Follow-up Period				
	Day -28 to -1	D1 ^b	D8	D15	D22	D29	D36	D43	D50	D57	Day 1 of each 21- Day Cycle (starting D64)	EOT ^c	30-Day FU	90-Day FU ^d	PD/ Survival	
Window (days)	-	+3	±3	±3	±3	±3	±3	±3	±3	±3	±3		±7	±7	±14	
Administer appropriate chemotherapy premedications	-	X	X	X	X	X	X	-	-	-	-	-	-	-	-	
CCI																
Administer radiotherapy ^e	-	60 Gy in 30 fractions (2 Gy per day/5 days per week)						-	-	-	-	-	-	-	-	-
Accountability tislelizumab/placebo	-	X	-	-	X		-	X	-	-	X	-	-	-	-	
Accountability paclitaxel/carboplatin	-	X	X	X	X	X	X	-	-	-	-	-	-	-	-	
FOLLOW-UP																
Survival follow-up	-	-	-	-	-	-	-	-	-	-	-	-	X	X	Every 3 months (± 14 days) until death	
Disease therapy since IP discontinuation	-	-	-	-	-	-	-	-	-	-	-	-	X	X	At every survival follow-up visit	

Abbreviations: AE = adverse event; ALK = anaplastic lymphoma kinase; β -hCG = beta human chorionic gonadotropin; CBC = complete blood count; cCRT = concurrent chemoradiotherapy; CK = creatine kinase; CK-MB = creatine kinase – cardiac muscle isoenzyme; CT = computed tomography; D = day; DNA = deoxyribonucleic acid; ECOG = Eastern Cooperative Oncology Group; EGFR = epidermal growth factor receptor; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer – Quality of Life C30 questionnaire; EOT = end of treatment; CCI [REDACTED] FDG-PET = fluorodeoxyglucose - positron emission tomography; FU = follow-up; Gy = gray; HBcAb = hepatitis B core antibody; HBsAb = hepatitis B surface antibody; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus HCV = hepatitis C virus; IP = investigational product; IRT = integrated response technology; MRI = magnetic resonance imaging; LC13 = Lung Cancer Module of EORTC QLQ-C30; OCT = optical coherence tomography; PD = progressive disease; CCI [REDACTED]; RNA = ribonucleic acid; RT = radiation therapy; SAE = serious adverse event; SOC = standard of care; 1 CCI [REDACTED]

- ^a Screening evaluations must be completed within 28 days of randomization.
- ^b Subjects should have Cycle 1 Day 1 (C1D1) dosing initiated within 3 days of randomization.
- ^c End of treatment visit to be completed as soon as possible after IP discontinuation decision.
- ^d The 90-Day Follow up Visit could be completed at the site or by telephone.
- ^e All AEs and SAEs, regardless of relationship to study treatment, will be reported until 30 days after last dose of study treatment. Immune-related AEs (serious or non-serious) should be reported until 90 days after the last dose of tislelizumab or placebo, regardless of whether or not the subject starts a new anticancer therapy. All AEs and SAEs considered related to RT will be collected at any time after the first dose of RT, including late radiation toxicities. After a subject has been discontinued from the study treatment, Investigators are not obligated to actively seek AEs or SAEs in former subjects. However, if the Investigator learns of any AE related to radiation or any SAE, and he/she considers the SAE related to the study drug, the Investigator will notify the sponsor as described in Section 10 of the protocol.
- ^f Vitals, weight, hematology and chemistry will be collected weekly during Cycles 1, 2, and 3.
- ^g Eye exam, visual acuity test, and optical coherence tomography (OCT) (or equivalent diagnostic test for retinal examination) captured as standard of care prior to obtaining written informed consent and within 28 days of randomization may be used rather than repeating tests. Eye exam, visual acuity test, and OCT (or equivalent diagnostic test) will be assessed at screening and then approximately every 15 weeks (\pm 7 days) during study treatment. The ophthalmologic assessments including eye exam, visual acuity test, and OCT (or equivalent diagnostic test) should only be performed once at either the EOT or during safety follow up, within 30 days of study treatment end.
- ^h Hematology, serum chemistry, coagulation and thyroid function laboratory tests will be performed centrally. Local laboratory tests can be used for enrollment and dosing day. If screening laboratory tests are performed within 3 days of C1D1, these tests do not need to be repeated on C1D1. Before any administration of study treatment on each cycle, the results of CBC and serum chemistry should be available and reviewed by the Investigator. Of note, creatine kinase (CK) and creatine kinase – cardiac muscle isoenzyme (CK-MB) will be assessed as part of the serum chemistry panel (as per Section 6). In case CK-MB fractionation is not available, please assess troponin (troponin I and/or T) instead.
- ⁱ Testing will be performed by a central laboratory and/or the local laboratory at screening and will include at screening HBV/HCV serology (HBsAg, HBsAb, HBcAb, and HCV antibody) and viral load assessment (HBV DNA and HCV RNA). After screening, HBV/HCV serology (HBsAg, HBsAb, HBcAb, and HCV antibody) and viral load assessment (HBV DNA and HCV RNA) may be performed if clinically indicated; for subjects who have detectable HBV DNA or HCV RNA at screening or upon repeat testing, respective viral load testing will be performed every 4 cycles (ie, Day 1 of Cycles 5, 9, 13, etc).
- ^j Urine pregnancy tests will be performed at each visit prior to dosing. A serum pregnancy test must be performed if the urine pregnancy test is positive or equivocal. CCI [REDACTED]
- ⁿ Cycle 3 Day 1 dosing may be delayed up to 7 days in order to ensure that cCRT is completed prior to the start of monotherapy with tislelizumab or placebo.
- ^o The schedule of radiotherapy and chemotherapy administrations is detailed in Table 5 of the protocol. Once commenced, radiotherapy should be given for 5 consecutive days weekly. Radiotherapy commences on Day 1 of chemotherapy, with a \pm 3 days administrative window allowed for Day 1 of each cycle only.

18.2. Handling of Dates

Dates will be stored as numeric variables in the SAS analysis files and reported in DDMMYYYY format (i.e., the Date9. datetime format in SAS). Dates in the clinical database are classified into the categories of procedure dates, log dates, milestone dates, outcome dates, and special dates.

- **Procedure Dates** are the dates on which given protocol-specified procedure are performed. They include the dates of laboratory testing, physical examinations, tumor scans, etc. They should be present whenever data for a protocol-specified procedure are present and should only be missing when a procedure are marked as NOT DONE in the database. Procedure dates will not be imputed.
- **Log Dates** are dates recorded in CRF data logs. Specifically, they are the start and end dates for adverse events and concomitant medications/procedures. They should not be missing unless an event or medication is marked as *ongoing* in the database. Otherwise, incomplete log dates will be imputed according to the rules in Appendix 16.3 (eg, for duration or cycle assignment, etc). However, in listings, log dates will be shown as recorded without imputation.
- **Milestone Dates** are dates of protocol milestones such as randomization, study drug start date, study drug termination date, study closure date, etc. They should not be missing if the milestone occurs for a subject. They will not be imputed.
- **Outcome Dates** are dates corresponding to study endpoints such as survival, progression, etc. In most cases they are derived either from a milestone (eg, the survival date is derived from the death date), or a procedure date (eg, the progression date is derived from the date of the tumor scan that was used to determine progression). They may be subject to endpoint-specific censoring rules if the outcome did not occur, but are not otherwise subject to imputation.
- **Special Dates** cannot be classified in any of the above categories and they include the date of birth. They may be subject to variable-specific censoring and imputation rules.

Dates recorded in comment fields will not be imputed or reported in any specific format.

18.2.1. Calculation Using Dates

Calculations using dates (e.g., subject's age or relative day after the first dose of study drug) will adhere to the following conventions:

- Study days after the start day of study drug will be calculated as the difference between the date of interest and the first date of dosing of study drug (e.g, tislelizumab or placebo) plus 1 day. The generalized calculation algorithm for relative day is the following:
 - If TARGET DATE \geq DRUG START DATE then STUDY DAY = (TARGET DATE – DRUG START DATE) + 1;

- Else use $\text{STUDY DAY} = \text{TARGET DATE} - \text{DRUG START DATE}$.

Note that Study Day 1 is the first day of treatment of study drug. Negative study days are reflective of observations obtained during the baseline/screening period. Note: Partial dates for the first study drug are not imputed in general. All effort should be made to avoid incomplete study drug start dates.

- Age (expressed in days) is calculated: $\text{AGE} = \text{CONSENT} - \text{DATE of BIRTH} + 1$. In practice, age will be transformed to years by dividing the difference by 365.25 days, then truncating.
 - Preference is for using calculated age from clinical database. When not available, calculated age from CRF or IVRS may be used
 - Partial birth date: impute missing day as 15th of the month; impute as 01-July for missing month; set missing age for missing year
- Intervals that are presented in weeks will be transformed from days to weeks by using (without truncation) the following conversion formula:

$$\text{WEEKS} = \text{DAYS} / 7$$

- Intervals that are presented in months will be transformed from days to months by using (without truncation) the following conversion formula:

$$\text{MONTHS} = \text{DAYS} / 30.4375$$

18.2.2. Calculation of Cycles

In this study, subjects meeting inclusion criteria will be randomized 1:1:1 via IVRS into 1 of 3 treatment arms to receive one of following study drugs:



Every 3 treatment weeks consist of a treatment cycle. The start date of each cycle will be calculated as follows:

A qualified cycle is defined as a CRF cycle during which the subject receives at least one dose of study drug. All qualified cycles will be sorted as the calculated cycle excluding CRF cycles during which the subject did not receive any study drug dose. The earlier dosing date (whether for tislelizumab, cCRT or placebo) will be considered the start data of the cycle.

18.3. Date Imputation Guideline

18.3.1. Impute Missing Adverse Events/ Prior or Concomitant Medications

Incomplete Start Date:

Missing day and month

- If the year is the same as the year of the first dosing date, then the day and month of the first dosing date will be assigned to the missing fields.
- If the year is prior to the year of first dosing date, then December 31 will be assigned to the missing fields.
- If the year is after the year of first dosing, then January 1 will be assigned to the missing fields.

Missing day only

- If the month and year are the same as the year and month of first dosing date, then the first dosing date will be assigned to the missing day.
- If either the year of the partial date is before the year of the first dosing date or the years of the partial date and the first dosing date are the same but the month of partial date is before the month of the first dosing date, then the last day of the month will be assigned to the missing day.
- If either the year of the partial date is after the year of the first dosing date or the years of the partial date and the first dose date are the same but the month of partial date is after the month of the first dosing date, then the first day of the month will be assigned to the missing day.
- If the stop date is not missing, and the imputed start date is after the stop date, the start date will be imputed by the stop date.

Missing day, month, and year

- No imputation is needed, the corresponding AE will be included as TEAE.

Incomplete Stop Date: If the imputed stop date is before the start date, then the imputed stop date will be equal to the start date.

Missing day and month

- If the year of the incomplete stop date is the same as the year of the last dosing date, then the day and month of the last dosing date will be assigned to the missing fields.
- If the year of the incomplete stop date is prior to the year of the last dosing date or prior to the year of the first dosing date, then December 31 will be assigned to the missing fields.
- If the year of the incomplete stop date is prior to the year of the last dosing date but is the same as the year of the first dosing date, then the first dosing date will be assigned to the missing date.

- If the year of the incomplete stop date is after the year of the last dosing date, then January 1 will be assigned to the missing fields.

Missing day only

- If the month and year of the incomplete stop date are the same as the month and year of the last dosing date, then the day of the last dosing date will be assigned to the missing day.
- If either the year of the partial date is not equal to the year of the last dosing date or the years of the partial date and the last dosing date are the same but the month of partial date is not equal to the month of the last dosing date, then the last day of the month will be assigned to the missing day.

18.3.2. Prior/Concomitant Procedures

Partially missing start dates for prior/concomitant procedures will be imputed in the ADaM dataset for prior/concomitant procedures.

Partially missing prior/concomitant medication/procedure start dates will be imputed by the earliest possible date given the non-missing field(s) of the date.

18.3.3. Medical History

Partially missing medical history start dates will be imputed in the ADaM dataset for medical history. The 16th of the month will be used to impute a partially missing start date that has only the day missing, and July 1st will be used to impute a partially missing start date that has both the month and day missing.



Celgene Signing Page

This is a representation of an electronic record that was signed electronically in Livelink.
This page is the manifestation of the electronic signature(s) used in compliance with
the organizations electronic signature policies and procedures.

UserName: PPD
Title: PPD
Date: Wednesday, 06 May 2020, 06:08 AM Eastern Daylight Time
Meaning: Approved, no changes necessary.
=====

UserName: PPD
Title: PPD
Date: Wednesday, 06 May 2020, 12:00 PM Eastern Daylight Time
Meaning: Approved, no changes necessary.
=====

UserName: PPD
Title: PPD
Date: Thursday, 07 May 2020, 08:23 AM Eastern Daylight Time
Meaning: Approved, no changes necessary.
=====

CELGENE PROPRIETARY INFORMATION