Protocol A7471064

SINGLE ARM STUDY TO EVALUATE THE SAFETY OF DACOMITINIB FOR THE FIRST-LINE TREATMENT OF PARTICIPANTS IN INDIA WITH METASTATIC NON-SMALL CELL LUNG CANCER WITH EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR)-ACTIVATING MUTATIONS

Statistical Analysis Plan
(SAP)

Version: **1**

Date: 01 Jun 2020

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1. VERSION HISTORY

This Statistical Analysis Plan (SAP) for study A7471064 is based on the protocol dated 01APR2020.

Table 1. Summary of Changes

Version/ Date	Associated Protocol Amendment	Rationale	Specific Changes
1 01 Jun 2020	Original 01 April 2020	N/A	N/A

2. INTRODUCTION

This SAP provides the detailed methodology for summary and statistical analyses of the data collected in Study A7471064. This document may modify the plans outlined in the protocol; however, any major modifications of the primary endpoint definition or its analysis will also be reflected in a protocol amendment.

Any deviations from this analysis plan will be described in the Clinical Study Report.

All summaries and analyses will include all data in the database at the end of study which is defined as 1 year after the last participant first visit date in the study.

2.1. Study Objectives, Endpoints, and Estimands

Objectives	Estimands	Endpoints
Primary		
• To assess safety and tolerability of dacomitinib	• The primary estimand is the incidence of Adverse Events (AEs) from the time of first dose to 28 days post last dosing date or the date of initiation of a new anticancer therapy, whichever occurs first for all participants who receive at least one dose of dacomitinib, regardless of dosing interruptions or dosing compliance.	• Incidence of AEs
Secondary		
• To evaluate antitumor activity	• The secondary estimand is the treatment effect of dacomitinib as	• Confirmed ORR and DoR as

of dacomitinib by Objective Response Rate (ORR) and Duration of Response (DoR)	assessed by the investigator from time of first dose (for ORR) or time of first tumor response (for DoR) until disease progression, death or initiation of a new anticancer therapy, whichever occurs first for all participants who receive at least one dose of dacomitinib without regard to tolerability or discontinuation from treatment	assessed by the investigator using Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1

2.1.1. Primary Estimand

The primary estimand is the incidence of adverse events from the time of first dose to 28 days post last dosing date or the date prior to initiation of a new anticancer therapy, whichever occurs first for all participants who receive at least one dose of dacomitinib, regardless of dosing interruptions or dosing compliance. It includes the following 4 attributes:

- Population: Participants with metastatic Non-Small Cell Lung Cancer (NSCLC) with EGFR exon 19 deletion or exon 21 L858R substitution mutations as defined by the inclusion and exclusion criteria, and who receive at least one dose of dacomitinib;
- Variable: Binary indicator of whether any AE occurred at least once;
- Intercurrent event(s): All data after the intercurrent event "initiation of a new anticancer therapy (-1 day)" or "treatment discontinuation (+28 days post last dosing date)" will be excluded. Dosing interruptions or dosing compliance are not considered as intercurrent event for this analysis;
- Population-level summary: Incidence of AEs defined as the number of participants with AEs from the time of first dose to 28 days post last dosing date or the date prior to initiation of a new anticancer therapy, divided by the number of participants in the Population.

2.1.2. Secondary Estimands

A secondary estimand is the treatment effect of dacomitinib based on ORR with confirmed response as assessed by the investigator from the time of first dose until disease progression, death or initiation of a new anticancer therapy, whichever occurs first for all participants who receive at least one dose of dacomitinib regardless of tolerability or duration on treatment. It includes the following 4 attributes:

- Population: Participants with metastatic NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution mutations as defined by the inclusion and exclusion criteria, and who receive at least one dose of dacomitinib;

- Variable: Confirmed objective response according to RECIST v1.1 per investigator, defined as Partial Response (PR) or Complete Response (CR) from the date of first dose until disease progression, death or initiation of a new anticancer therapy, whichever occurs first;

- Intercurrent event: All tumor assessments are considered regardless of gaps in assessments. All data after the intercurrent event "initiation of a new anticancer therapy" will be excluded. Dosing interruptions and dosing compliance are not considered as intercurrent event for this analysis;

- Population-level summary: ORR, ie percentage of participants with confirmed CR or confirmed PR and corresponding 95% confidence interval (CI) based on Wilson's Score Method.

Another secondary estimand is the treatment effect of dacomitinib based on DoR from the time of first tumor response until disease progression, death or initiation of a new anticancer therapy, whichever occurs first for all participants who receive at least one dose of dacomitinib and who show a confirmed objective response per investigator, regardless of tolerability or duration on treatment. It includes the following 4 attributes:

- Population: Participants with metastatic NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution mutations as defined by the inclusion and exclusion criteria, and who receive at least one dose of dacomitinib and showing a confirmed OR per investigator;

- Variable: DoR;

- Intercurrent event: All data after the intercurrent events "initiation of a new anticancer therapy" or "extended gap in tumor assessment, defined as 2 or more missed tumor assessments prior to disease progression or death" will be excluded. Dosing interruptions and dosing compliance are not considered as intercurrent event for this analysis;

- Population-level summary: Kaplan-Meier Median of DoR and 2-sided 95% CI.

2.1.3. Additional Estimand(s)

Not applicable.

2.2. Study Design

This is a Phase 4, open-label, single arm, multicenter, prospective clinical trial of dacomitinib for the first-line treatment of newly diagnosed adult participants with metastatic NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution mutations. This study will enroll a sufficient number of participants to ensure that 100 participants are treated with dacomitinib.

Participants will continue with the study treatment until disease progression, participant refusal/lost to follow-up, or unacceptable toxicity. At the end of the study, participants who are on treatment and benefiting from dacomitinib treatment will be switched to commercially available dacomitinib if considered appropriate by the investigator, as soon as feasible.

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoint

The primary endpoint is the incidence of AEs, defined as the number of participants with treatment-emergent adverse events (TEAEs) from the time of first dose to 28 days post last dosing date or the date prior to initiation of a new anticancer therapy, divided by the number of participants in the Safety Set (see Section 4).

An adverse event is considered treatment-emergent if any of the following apply:

- The event occurs on-treatment (defined in Section 3.5) and was not seen prior to the start of treatment.
- The event was seen prior to the start of treatment but increased in National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v4.03 grade while on-treatment.

Treatment-emergent adverse events will be characterized by type, frequency, severity (as graded by the investigator according to NCI CTCAE version 4.03 and coded by the Sponsor using Medical Dictionary for Regulatory Activities [MedDRA]), timing, seriousness, and relationship to dacomitinib.

3.2. Secondary Endpoints

3.2.1. Overall Response Rate

Objective response based on investigator assessment is defined as CR or PR according to RECIST v1.1. Both CR and PR must be confirmed by repeat assessments performed no less than 4 weeks after the criteria for response are first met. Participants without a CR or PR or with death prior to first post-baseline assessment, inadequate baseline assessment, new anticancer therapy started prior to first post-baseline assessment, and all post-baseline disease assessments missing will be considered as non-responders.

The Best Overall Response (BOR) is the best response recorded from date of first dose until documented Progressive Disease (PD) or start of new anticancer therapy without regard to tolerability or discontinuation from treatment. Additional details are provided in Section 6.2.1.

The Overall Response Rate (ORR) is defined as the proportion of participants with a BOR characterized as either a CR or PR relative to the Safety Set.

3.2.2. Duration of Response

DoR based on investigator assessment is defined, for participants with a confirmed objective response, as the time from first documentation of objective response (CR or PR per RECIST v1.1, whichever is earlier) to the date of first documentation of PD or death due to any cause, whichever occurs first. The censoring rules for DoR are presented in Section 6.2.2.

3.3. Other Endpoint(s)

Not applicable.

3.4. Baseline Variables

Start and end dates of study treatment:

The date of first dose (start date) of study treatment is the earliest date of non-zero dosing of the study drug.

The date of last dose of study treatment is the latest date of non-zero dosing of the study drug.

Definition of baseline:

No windowing will be applied when defining baseline. Any deviations from the protocol specified window will be documented as protocol deviations. A separate definition of adequate baseline will be provided for antitumor activity endpoints.

For antitumor activity analyses and baseline characteristics associated with tumor assessments, the last assessment prior to date of the first dose of study treatment will serve as the baseline assessment.

For safety (including Eastern Cooperative Oncology Group (ECOG) performance status), the last assessment performed on or prior to date of the first dose of study treatment will serve as the baseline assessment. If there are no observations meeting these criteria, then baseline is considered missing.

Participants who start treatment and discontinue from the study on the same day may have two different sets of data collected on study day 1 (one during study and one in the End of Treatment (EOT) visit. Data reported at the EOT visit are not eligible for baseline selection.

Triplicate electrocardiograms (ECGs) are collected pre-dose; therefore the baseline for each ECG measurement is the average of the pre-dose measurements.

3.5. Safety Endpoints

Safety endpoints will be summarized based on the on-treatment period unless otherwise specified.

On-treatment is defined as the time from the first dose of study treatment through end of study follow-up (ie, 28 days after last dose) or the date prior to initiation of a new anticancer therapy, whichever occurs first. The start of new anticancer therapy after the first dose of study treatment is derived as outlined in Section 5.2.3. Adverse events occurring on the same day as the first dose of study treatment will be considered to have occurred during the on-treatment period. All other assessments which occur on the same day as the first dose of study treatment will be considered baseline assessments (see Section 3.4 for baseline definition).

Safety data collected outside the on-treatment period will be listed but not summarized.

3.5.1. Laboratory Data

Hematology and chemistry result will be programmatically graded according to the NCI CTCAE version 4.03 for relevant parameters. A shift summary of baseline grade by maximum post-baseline grade will be presented. Parameters which cannot be graded will be summarized relative to the normal range (ie, normal range high or normal range low). Additional details are provided in Section 6.6.1.

3.5.2. Vital Signs

Vital signs data include weight, pulse rate, systolic blood pressure, and diastolic blood pressure. Measurements were only to be provided once per timepoint. If multiple assessments are provided per timepoint, the maximum value will be used for reporting. Additional details are provided in Section 6.6.2.

3.5.3. Electrocardiograms

Three consecutive 12-lead ECGs pre-dose will be performed approximately 2 minutes apart to determine mean HR, RR, QT interval, PR interval, QRS complex, and QTcF at baseline. Additional ECGs may be collected as clinically indicated and as single ECGs. All ECG recordings will be listed. However, only the mean score calculated for the replicate measurements will be summarized. Additional details are provided in Section 6.6.3.

4. ANALYSIS SETS (POPULATIONS FOR ANALYSIS)

Data for all participants will be assessed to determine if participants meet the criteria for inclusion in each analysis population prior to releasing the database and classifications will be documented per standard operating procedures.

Only participants who signed informed consent will be included in the analysis sets below.

Population	Description
Enrolled	All participants who sign the informed consent document.
Safety	All participants who receive at least 1 dose of dacomitinib.

5. GENERAL METHODOLOGY AND CONVENTIONS

All analyses will be performed at study participant data set release at the end of study, defined as 1 year after the last participant first visit (LPFV) date in the study.

5.1. Hypotheses and Decision Rules

5.1.1. Hypotheses and Sample Size

This is a single arm study with no statistical hypothesis testing. The primary objective of the trial is to evaluate the safety and tolerability of single-agent dacomitinib for the first-line treatment of participants in India with metastatic NSCLC with EGFR activating mutations.

This study will enroll a sufficient number of participants to ensure that 100 participants are treated with dacomitinib.

5.1.2. Decision Rules

Not applicable.

5.2. General Methods

5.2.1. Definition of Study Day

The study day for assessments occurring on or after the first dose of study treatment (eg, adverse event onset, tumor measurement) will be calculated as:

Study day = Date of the assessment/event - start date of study treatment + 1.

The study day for assessments occurring prior to the first dose of study treatment (eg, baseline characteristics, medical history) will be negative and calculated as:

Study day = Date of the assessment/event - start date of study treatment.

The study day will be displayed in all relevant data listings.

5.2.2. Definition of Cycle and Cycle Day

Cycle start and end dates are derived per participant. Treatment will be dispensed at the beginning of every 28-day cycle.

- For Cycle X, the actual cycle start date for each participant is:
  - The earliest start date of dosing (dose>0 at that visit) in Cycle X visit case report form (CRF) exposure page.

- For all but the last cycle.
    - Actual cycle stop date is calculated as the start date of the next cycle minus one day.
    - Actual cycle duration is calculated from Day 1 of a cycle to the day prior to Day 1 of the next cycle, as follows:

        Actual Cycle Duration (weeks) = (cycle stop date – cycle start date +1)/7.

- For the last cycle, actual cycle duration is calculated as follows:
    - Actual Cycle Duration (weeks) = (last date of study treatment– cycle start date +1)/7.

The cycle day will be calculated as:

Cycle day = Date of the assessment/event – cycle start date + 1.

5.2.3. Definition of Start of New Anticancer Therapy

Start date of new anticancer therapy (drug, radiation, surgery) is used to determine the end of the on-treatment period (see Section 3.5) and for censoring in antitumor activity analyses (see Section 6.2).

The start date of new anticancer therapy is the earliest date after first dose of dacomitinib amongst the following:

- Start date of anticancer drug therapy recorded in the 'Concomitant Medications' CRF pages with 'Category of medication' = 'Follow-up Cancer Therapy';
- Start date of radiation therapy recorded in 'Radiation Treatment' CRF pages with 'Subcategory' = 'Curative in intent';
- Surgery date recorded in 'Non-drug Treatments' CRF pages with 'Category' = 'On-study Cancer Surgery' and 'Outcome of Procedure' = 'Resected' or 'Partially Resected'.

When start date of anticancer therapy is missing or partially missing, the imputation rules described in Section 5.3.2.4 should be applied using 'Concomitant Medications', 'Radiation Treatment', and 'Non-drug Treatments' CRF pages.

5.2.4. Date of Last Contact

The date of last contact will be derived for participants not known to have died at the end of study using the latest complete date (ie, imputed dates will not be used in the derivation) among the following:

- All participant assessment dates eg, tumor assessments;

- Start and stop dates of concomitant therapies including non-drug treatments or procedures;
- Start and end dates of anticancer therapies administered after study treatment discontinuation including systemic therapy, radiation, and surgeries;
- AE start and end dates;
- Date of first and last dose;
- Vital sign, ECG and laboratory assessment;
- Date of discontinuation on disposition CRF pages (do not use if reason for discontinuation is lost to follow-up or death).

Only dates associated with actual examinations of the participant will be used in the derivation. Assessment dates after the end of study will not be applied to derive the last contact date.

5.2.5. Tumor Assessment Date

The date of tumor assessment at each nominal timepoint as provided by the investigator on the Investigator Overall Tumor Assessment (IOTA) CRF will be utilized for the antitumor activity analyses.

5.2.6. Adequate Baseline Tumor Assessment

Adequate baseline is defined using the following criteria:

- All baseline assessments must be within 35 days prior to and including the date of first dose of dacomitinib.
- All documented lesions must have non-missing assessments (ie, non missing measurements for target lesions and non missing lesions status at baseline for non-target lesions).
- Measurable disease at baseline, defined as at least one non-nodal target lesion with longest diameter $\geq$10 mm by computerized tomography (CT) or magnetic resonance imaging (MRI) or calliper for superficial lesion, or at least one malignant lymph node with short axis $\geq$15mm.

5.2.7. Adequate Post-baseline Tumor Assessment

An adequate assessment is defined as an assessment where a response of CR, PR, Stable Disease (SD), non-CR/non-PD, or PD has been provided by the investigator. Timepoints where the response is not evaluable or no assessment was performed will not be used for determining the censoring date.

5.2.8. Nominal and Unscheduled Visits

For all algorithms and analyses, visit labels as specified on the CRF will be used as the nominal timepoint (ie, assessment will not be slotted).

Unless otherwise specified, unscheduled assessments will not be displayed in summary tables by nominal visit/timepoint. Unscheduled assessments will be used when deriving baseline and worst case on-treatment for adverse events, laboratory and vital signs assessments. Additionally, unscheduled tumor assessments will be used for antitumor activity analyses (eg, defining date of progression/censoring, best overall response, date of last contact).

5.2.9. Standard Derivations and Reporting Conventions

The following conversion factors will be used to convert days into weeks, months or years: 1 week = 7 days, 1 month = 30.4375 days, 1 year = 365.25 days.

Demographics and physical measurements:

- Age [years]:
    - (year of given informed consent - year of birth).

For reporting conventions, mean and median should generally be displayed one more decimal place than the raw data and standard deviation (Std Dev) should be displayed to two more decimal places than the raw data. Percentages will be reported to one decimal place. The rounding will be performed to closest integer/first decimal using the common mid-point between the two consecutive values eg, 5.1 to 5.4 will be rounded to an integer of 5, and 5.5 to 5.9 will be rounded to an integer of 6.

5.2.10. Analyses for Continuous and Qualitative Variables

Continuous variables will be summarized using descriptive statistics ie, number of non-missing values and number of missing values [ie, n (missing)], mean, median, Std Dev, minimum, maximum and first and third quartile (Q1 and Q3).

Qualitative variables will be summarized by frequency counts and percentages. Unless otherwise specified, the calculation of proportions will include the missing category. Therefore counts of missing observations will be included in the denominator and presented as a separate category.

In case the analysis refers only to certain visits, percentages will be based on the number of participants still present in the study at that visit, unless otherwise specified.

5.2.11. Analyses for Time-to-Event Endpoints

Time to event endpoint will be summarized using the Kaplan-Meier method and estimated survival curves will be displayed graphically if appropriate. The median event time (if appropriate) and 2-sided 95% CI for the median will be provided based on the Brookmeyer-Crowley method. In case the number of participants with PD after a confirmed CR or confirmed PR is small for the Kaplan-Meier method, descriptive statistics will be provided.

5.3. Methods to Manage Missing Data

Unless otherwise specified, all data will be evaluated as observed, and no imputation method for missing values will be used.

Any imputations will occur at the analysis dataset level. Additionally, in all data listings imputed values will be presented and flagged as imputed.

Missing statistics, eg, when they cannot be calculated, should be presented as 'ND' for not done, 'NR' for not reached or 'NA' for not applicable. For example, if N=1, the measure of variability cannot be computed and should be presented as 'ND' or 'NA'.

5.3.1. Missing ECG Data

For QTc analyses, no values will be imputed for missing data. If one or two of the triplicate measurements for an ECG parameter are missed, the average of the remaining two measurements or the single measurement can be used in the analyses. If all triplicate measurements are missing at baseline for an ECG parameter, no values will be imputed.

5.3.2. Handling of Incomplete or Missing Dates

5.3.2.1. Adverse Events

AE Onset Date:

The following imputation rules apply if the event is unique for a participant or it is the first of a series of similar events; otherwise, the AE Onset Date will not be imputed:

- If the AE Collection Date is not missing, is less than the Date of First Exposure to Treatment, and is less than the AE Stop Date, then AE Onset Date is set to the Date of AE Collection.
- If the Previous Visit Date is greater than the Date of First Exposure to Treatment and less than the AE Stop Date, the AE Onset Date is set to the previous visit date.
- If the Date of First Exposure to Treatment is greater than the previous visit date and less than the AE Stop Date, the AE Onset Date is set to the Date of First Exposure to Treatment.
- Otherwise AE Onset date is set to the AE Stop date.

AE Stop Date:

Ongoing events will have the AE Stop Date set to one of the following values:

- Date of Death, if the participant died and a date of death exists.
- Maximum of (Withdraw date, AE Onset Date, AE Collection Date) if the participant withdrew from the study and a date of withdraw exists.

- Maximum of (AE Onset Date, Subject Summary Collection Date, AE Collection Date) if the Subject Summary CRF page exists but a date of withdraw does not exists.

- Maximum of (Last Treatment Date, AE Onset Date) if no Subject Summary page exits.

Imputation will only occur if event is unique for the participant, or it is the last of a series of similar events; otherwise the Stop Date will not be imputed. Adverse Events are deemed similar if they have the same verbatim term.

Resolved events will have the AE Stop Date set to the maximum of the AE collection date and the AE Onset date.

5.3.2.2. Exposure

No imputation will be done for first dose date. Date of last dose of study treatment, if unknown or partially unknown, will be imputed as follows:

- If the last date of study treatment is completely missing and there is no EOT CRF page and no death date, the participant should be considered to be ongoing and use the data cutoff date for the analysis as the last dosing date; or

- If the last date of study treatment is completely or partially missing and there is EITHER an EOT CRF page OR a death date available (on or prior to the data cutoff date), then impute this date as the last dose date:

  = 31DECYYYY, if only Year is available and Year < Year of min (EOT date, death date),

  = Last day of the month, if both Year and Month are available and Year = Year of min (EOT date, death date) and Month < the month of min (EOT date, death date), or

  = min (EOT date, death date), for all other cases.

5.3.2.3. Date of Death

Missing or partial death dates will be imputed based on the last contact date:

- If the date is missing it will be imputed as the day after the date of last contact

- If the day or both day and month is missing, death will be imputed to the maximum of the full (non-imputed) day after the date of last contact and the following:

  - Missing day: 1st day of the month and year of death;

  - Missing day and month: January 1st of the year of death.

5.3.2.4. Date of Start of New Anticancer Therapy

Incomplete dates for start date of new anticancer therapy (drug therapy, radiation, surgery) will be imputed as follows and will be used for determining censoring dates for antitumor activity analyses and in the derivation of the end of on-treatment period. PD date below refers to PD date by investigator assessment.

- The end date of new anticancer therapy will be included in the imputations for start date of new anticancer therapy. If the end date of new anticancer therapy is:
  - Completely missing then it will be ignored in the imputations below;
  - Partially missing with only year (YYYY) available then the imputations below will consider 31DECYYYY as the end date of the new anticancer therapy;
  - Partially missing with only month and year available then the imputations below will consider the last day of the month for MMMYYYY as the end date of the new anticancer therapy.
- For participants who have not discontinued study treatment at the analysis cutoff date, last dose of study treatment is set to the analysis cutoff date in the imputations below.
- If the start date of new anticancer therapy is completely or partially missing then the imputed start date of new anticancer therapy is derived as follows:
  - Start date of new anticancer therapy is completely missing.

    Imputed start date = min [max(PD date +1, last dose of study treatment +1), end date of new anticancer therapy].
  - Only year (YYYY) for start of anticancer therapy is available.

    IF YYYY < Year of min [max(PD date +1, last dose of study treatment +1), end date of new anticancer therapy] THEN imputed start date = 31DECYYYY.

    ELSE IF YYYY = Year of min [max(PD date +1, last dose of study treatment +1), end date of new anticancer therapy].

    THEN imputed start date = min [max(PD date +1, last dose of study treatment +1), end date of new anticancer therapy].

    ELSE IF YYYY > Year of min [max(PD date +1, last dose of study treatment +1), end date of new anticancer therapy].

    THEN imputed start date = 01JANYYYY.
  - Both Year (YYYY) and Month (MMM) for start of anticancer therapy are available.

IF

YYYY = Year of min [max(PD date + 1, last dose of study treatment +1), end date of new anticancer therapy], AND

MMM < Month of min [max(PD date + 1 day, last dose of study treatment +1 day), end date of new anticancer therapy].

THEN

imputed start date = DAY (Last day of MMM) MMM YYYY.

ELSE IF

YYYY = Year of min [max(PD date +1, last dose of study treatment +1), end date of new anticancer therapy], AND

MMM = Month of min [max(PD date +1 day, last dose of study treatment +1 day), end date of new anticancer therapy].

THEN

imputed start date = min [max(PD date + 1 day, last dose of study treatment +1 day), end date of new anticancer therapy]).

ELSE IF

YYYY = Year of min [max(PD date +1, last dose of study treatment +1), end date of new anticancer therapy], AND

MMM > Month of min [max(PD date +1 day, last dose of study treatment +1 day), end date of new anticancer therapy].

THEN

imputed start date = 01 MMM YYYY.

ELSE IF

YYYY < Year of min [max(PD date + 1, last dose of study treatment + 1), end date of new anticancer therapy].

THEN

imputed start date = DAY (Last day of MMM) MMM YYYY.

ELSE IF

YYYY > Year of min [max(PD date + 1, last dose of study treatment + 1), end date of new anticancer therapy].

THEN.

imputed start date = 01 MMM YYYY.

5.3.2.5. Other Dates

Imputation methods for other partial dates as follows:

- If the day of the month is missing for a start date used in a calculation, the first day of the month will be used to replace the missing date.
- If both the day and month are missing, the first day of the year is used.
- For stop dates, the last day of the month, or last day of the year is used if the day or day and month are missing, respectively.
- If the date is completely missing, no imputation will be performed.

5.3.3. Missing Toxicity Grade of Adverse Events

Prior to Study Treatment: If no toxicity grade is available or the grade is reported as unknown for an adverse event prior to the first study treatment, then Grade 1 will be assumed for purposes of defining a baseline grade.

In summaries which present maximum toxicity grade, the maximum of non-missing grades will be displayed. Missing grade will only be displayed for cases where a participant reported only one event and the grade is missing.

6. ANALYSES AND SUMMARIES

6.1. Primary Endpoint(s)

6.1.1. Adverse Events

Analyses of adverse events will be conducted on the Safety Set and will include all data collected from the time of first dose to 28 days post last dosing date or the date prior to initiation of a new anticancer therapy, regardless of dosing interruptions or dosing compliance. All analyses will be based on treatment emergent events unless otherwise specified. Treatment emergent is defined in Section 3.1. AEs not considered treatment emergent will be flagged in data listings.

A high level summary of adverse events will include the number and percent of participants with:

- Any Adverse Event;
- Serious AE;
- Adverse Events with CTCAE Grade 3-4;
- Grade 5 events;
- AEs associated with dose interruptions;

- AEs associated with dose reductions;
- AEs associated with withdrawal.

Additionally, the number of events reported for each of the categories above will be provided. Each unique adverse event at the Preferred Term (PT) level for a participant is included in the count.

Seriousness, toxicity grade, action taken (interruption, reduction, and withdrawal) are as reported by the investigator on the adverse event CRF.

Summaries by System Organ Class (SOC) and PT in decreasing frequency will be provided for:

- Treatment Emergent Events (All Causality);
- Treatment Emergent Events by Maximum Toxicity Grade (All Causality);
- Treatment Emergent Events (Treatment Related);
- Treatment Emergent Events by Maximum Toxicity Grade (Treatment Related);
- Serious Treatment Emergent Events (All Causality);
- Serious Treatment Emergent Events (Treatment Related).

An event will be considered treatment related if the investigator considered the event related to the study drug or if causality information is unknown.

The following summaries will be provided by PT only (ie, summaries will not include SOC) in decreasing frequency for:

- Treatment Emergent Events (All Causality) by Preferred Term and Maximum Toxicity Grade;
- Treatment Emergent Grade 3-5 Events (All Causality) by Preferred Term and Maximum Toxicity Grade;
- Treatment Emergent Adverse Events Leading to Dose Interruptions (All Causality);
- Treatment Emergent Adverse Events Leading to Dose Interruptions (Treatment Related);
- Treatment Emergent Adverse Events Leading to Dose Reductions (All Causality);
- Treatment Emergent Adverse Events Leading to Dose Reductions (Treatment Related);

- Treatment Emergent Adverse Events Leading to Permanent Withdrawal of Study Drug (All Causality);
- Treatment Emergent Adverse Events Leading to Permanent Withdrawal of Study Drug (Treatment Related);
- Serious Treatment Emergent Events (All Causality); and
- Serious Treatment Emergent Events (Treatment Related).

Each participant will be counted only once within each SOC and PT.

As described in Section 5.3.3, in case a participant has events with missing and non missing toxicity grades, the maximum of the non-missing grade will be displayed. Missing grade will only be displayed in the event that only one event has been reported for a participant and the grade is missing.

6.2. Secondary Endpoint(s)

6.2.1. Overall Response Rate

Analysis of treatment effect based on Overall Response Rate (ORR) will be conducted on the Safety Set and will include all data collected from the time of first dose until disease progression, death or initiation of a new anticancer therapy, whichever occurs first, regardless of tolerability or duration on treatment.

ORR is defined as the percentage of participants with a best overall confirmed response of CR or PR according to RECIST v1.1. Participants without documented CR or PR will be considered as non-responders. The evaluation of ORR will be based on investigator assessment relative to the Safety Set.

ORR will be calculated along with the two-sided 95% CI using the Wilson's Score Method.

In addition, the frequency (number and percentage) of participants with BOR of CR, PR, SD, PD, non-CR/non-PD (applicable only to participants with non-measurable disease at baseline), and NE (not-evaluable) will be tabulated.

BOR will be assessed based on reported overall responses at different evaluation timepoints by the investigator from the date of first dose until documented disease progression or start of new anticancer therapy, according to the following rules:

- CR = at least two determinations of CR at least 4 weeks apart and documented before progression and start of new anticancer therapy
- PR = at least two determinations of PR or better (and not qualifying for a CR) at least 4 weeks apart and before progression and start of new anticancer

- SD (for participants with at least one measurable lesion at baseline) = at least one SD assessment (or better and not qualifying for CR or PR) ≥ 6 weeks after date of first dose and before progression and the start of new anticancer therapy

- Non-CR/Non-PD (for participants with only non-target disease at baseline) = at least one Non-CR/Non-PD assessment (or better and not qualifying for CR) ≥ 6 weeks after date of treatment start and before progression and the start of new anticancer therapy

- PD = progression ≤ 13 weeks after date of first dose and not qualifying for CR, PR or SD

- Not Evaluable (NE) = all other cases.

Clinical deterioration will not be considered as documented disease progression.

Participants with BOR of NE will be summarized by reason for having NE status. The following reasons will be used:

- Early death (defined as death prior to 6 weeks after date of first dose;

- No post-baseline assessments, for reasons other than early death;

- All post-baseline assessments have overall response NE;

- New anticancer therapy started before first post-baseline assessment;

- SD of insufficient duration (< 6 weeks after first dose);

- PD too late (> 13 weeks after first dose).

Special and rare cases where BOR is NE due to both early SD and late PD will be classified as 'SD of insufficient duration'.

6.2.2. Duration of Response

Analysis of treatment effect based on Duration of Response (defined in Section 3.2.2) will be conducted on participants from the Safety Set with a BOR of CR or PR and will include all data collected from the time of tumor response until disease progression, death or initiation of a new anticancer therapy, whichever occurs first, regardless of tolerability or duration on treatment.

DoR will be calculated as follows:

> DoR (months) = [first date of PD or death/censoring – first date of CR/PR subsequently confirmed+1]/30.4375.

DoR data will be censored as follows:

- For participants who start a new anticancer therapy prior to an event (PD or death), censoring will be at the last adequate tumor assessment (see Section 5.2.7) prior to the start of new anticancer therapy. Note: if date of progression occurs on the same date as the start of new anticancer therapy, the progression will be counted as an event.

- For participants with documented progression or death after two or more missing tumor assessments, censoring will occur at the last adequate tumor assessment prior to the missing assessments. In this study antitumor activity will be assessed through radiological tumor assessments conducted at screening and every 12 weeks until disease progression regardless of initiation of subsequent anticancer therapy. The allowable time window for disease assessments is ±1week while on treatment. Therefore time without adequate assessment is defined as 24 weeks plus 2 weeks.

- All other participants alive without objective progression will be censored on the date of the last adequate tumor assessment.

The date of tumor response at each nominal timepoint based on the investigator assessments will be used for determining the dates of last adequate assessment for censoring purposes.

The censoring and event date options to be considered for the DoR analysis are presented in Table 2.

Table 2. Outcome and Event Dates for DoR Analyses

Scenario	Date of event/censoring	Outcome
Progression or death ≤26 weeks after last adequate tumor assessment	Date of progression or death	Event
Progression or death >26 weeks after the last adequate tumor assessment	Date of last adequate assessment documenting no PD prior to new anticancer therapy or missed assessments	Censored
No progression		
New anticancer therapy given prior to PD		

Kaplan-Meier estimates (product-limit estimates) will be presented together with a summary of associated statistics including the median DoR time with two-sided 95% CIs. The CIs for the median will be calculated according to Brookmeyer and Crowley. When the number of participants with PD after a confirmed CR or PR is small, the use of Kaplan-Meier method is limited due to high number of censored observation, so the DoR will be summarized using number (%) of participants with events and of participants censored with DoR in the following categories: less than 6 months, ≥6 - <9 ,≥9-<12, ≥12-<15, ≥15-<18, ≥18-<21, ≥21-<24, and ≥24 months.

Frequency (number and percentage) of participants with each event type (PD or death) and censoring reasons will be presented along with the overall event and censor rates.

Reasons for censoring will be summarized according to the categories in Table 3. If a participant meets multiple definitions for censoring the list will be used to define the hierarchy.

Table 3. Censoring Reasons and Hierarchy for DoR Analyses

Hierarchy	Condition	Censoring Reason
1	Start of new anticancer therapy before event.	Start of new anticancer therapy
2	Event more than 26 weeks from last adequate post-baseline tumor assessment	Event after missing assessments [a]
3	No event and [withdrawal of consent date ≥ first date of CR/PR or End of study (EOS) = Subject refused further follow-up]	Withdrawal of consent
4	No event and lost to follow-up in any disposition page	Lost to follow-up
5	No event and none of the conditions in the prior hierarchy are met	Ongoing without an event

[a] more than 26 weeks after last adequate tumor assessment.

6.3. Other Endpoint(s)

Not applicable.

6.4. Subset Analyses

Not applicable.

6.5. Baseline and Other Summaries and Analyses

6.5.1. Baseline Summaries

6.5.1.1. Demographic Characteristics

The following demographic and baseline characteristics will be summarized by number and percentage:

- Gender (male, female);
- Age (18-<45; 45- <65; ≥65);
- Eastern Cooperative Oncology Group (ECOG) Performance status.

Age (continuous) and weight (kg) will be summarized with descriptive statistics (mean, median, Std Dev, minimum, and maximum).

6.5.1.2. Medical History

Medical history will be coded using the most current version of MedDRA and summarized by MedDRA's SOC and PT from the 'Medical History' CRF page. Each participant will be counted only once within each PT or SOC. Summaries will be ordered by primary SOC and PT in descending order of frequency. Separate summaries will be provided for past and present conditions.

6.5.1.3. Disease Characteristics

The following baseline disease characteristics will be summarized by number and percentage:

- Measurable disease at baseline (yes/no);
- Involved tumor sites at baseline;
- Number of sites of disease at baseline (1, 2, ≥3).

Involved tumor sites at baseline will be derived from target and non target lesions at baseline. Each participant will be counted once per organ. Similarly, number of sites of disease at baseline will be derived by counting the number of unique organ sites from target and non target lesions at baseline. "Other" will be counted as one organ site.

6.5.1.4. Prior Anticancer Therapy

The prior anticancer therapies are collected under the 'Response to Regimen', 'Prior Radiation Therapy' and 'Non-drug Treatments' (with 'Category' = 'Prior Cancer Surgery') CRF pages.

The number and percentage of participants in each of the following anticancer therapy categories will be tabulated:

- Participants with at least one type of prior anticancer treatment;
- Participants with at least one prior anticancer drug therapy;
- Participants with at least one prior anticancer radiotherapy;
- Participants with at least one prior anticancer surgery.

Prior anticancer drug therapy will be summarized as follows based on the number and percentage of participants:

- Number of prior anticancer therapy regimens: missing /1/2/3/≥4;
- Type of prior anticancer therapy;

- Intent of Therapy: Neo-Adjuvant / Adjuvant / Advanced – Metastatic.

The prior anticancer drugs will be coded in the World Health Organization (WHO) Drug coding dictionary.

6.5.2. Study Conduct and Participant Disposition

6.5.2.1. Disposition

A summary of the number of participants enrolled by site will be provided for the Enrolled Set.

Discontinuations from study (overall and by main reason for study discontinuation) will be summarized using the Enrolled Set. Discontinuations from study treatment (overall and by main reason for study treatment discontinuation) will be summarized using the Safety Set.

Discontinuations from study treatment due to adverse events will be identified as either related or not related to study treatment. If causality is missing, the event will be considered related to treatment. If multiple events lead to study treatment discontinuation and at least one was considered related, discontinuation will be reported as related to study treatment.

6.5.2.2. Protocol Deviations

Protocol deviations will be compiled prior to database closure and will be summarized by category (n(%)) for the Enrolled Set. Categories will be assigned by the study Clinician.

6.5.3. Study Treatment Exposure

Exposure will be summarized for the Safety Set.

6.5.3.1. Exposure to dacomitinib

The summary of treatment exposure for dacomitinib will include the following information:

- Treatment duration (weeks);
- Cumulative dose (mg);
- Dose intensity (mg/week);
- Relative dose intensity (%).

The duration of dacomitinib (in weeks) is defined as:

Treatment duration (weeks) = (last dose date – first dose date +1)/7.

The cumulative dose (mg) of dacomitinib is the sum of the actual dose levels that the participant received (ie, total dose administered (mg)).

The dose intensity (DI) and the relative dose intensity (RDI) of dacomitinib will be calculated for each participant during the study. The DI (mg/week) of dacomitinib is defined as:

DI (mg/week) = [cumulative dose (mg)]/[treatment duration (weeks)].

The RDI of dacomitinib is defined as the ratio of the DI and planned dose intensity (d) and expressed in %.

RDI (%) = 100× [DI (mg/week]/[7×d (mg/week)].

6.5.3.2. Dose Reductions, Interruptions, and Delays

A dose reduction is defined as a non-zero dose that is less than the prior dose.

The number and percentage of participants with at least one dose reduction as well as a breakdown of dose reductions (1/2/3/≥4) will be summarized.

Reasons for dose reductions will also be summarized. Participants can contribute to more than one reason if multiple dose reductions occurred for different reasons, but will only be counted once per reason. Percentages will be calculated based on the total number of participants in Safety Set.

An interruption is defined as 0 mg dose administered on one or more days. (Note: A dose interruption is not considered a dose reduction). The number and percentage of participants with dose interruptions and the corresponding reasons will be summarized. Participants can contribute to more than one reason if multiple dose interruptions occurred for different reasons, but will only be counted once per reason. Percentages will be calculated based on the total number of participants in Safety Set.

The following defines how dose interruptions will be counted in the case of multiple dose interruptions:

- If an interruption occurs consecutively for at least two days due to the same reason, then it will be counted only once.
- If an interruption occurs consecutively for at least two days due to different reasons, then it will be counted for each reason
- If an interruption occurs for more than one day due to the same reason, but the days are not consecutive, ie. there is at least one dosing day in between, then each dose interruption will be counted as a different occurrence.

6.5.4. Concomitant Medications and Nondrug Treatments

The following analyses will be based on the Safety Set.

Concomitant medications are medications, other than study medications, which started prior to first dose date of study treatment and continued on on-treatment period as well as those started during the on-treatment period. Concomitant non-drug treatments refer to concurrent procedures, which were undertaken any time during the on-treatment period. Prior medications and prior non-drug treatments are medications/procedures which are started before the first dose of study treatment. Prior and concomitant medications will be coded in the WHO Drug coding dictionary. Prior and concomitant non-drug treatments will be coded with the most current version of MedDRA dictionary.

Summary of prior and concomitant medications will include the number and percentage of participants by Anatomical Therapeutic Chemical (ATC) Classification level 2 and preferred term. A participant will be counted only once within a given drug class and within a given drug name, even if he/she received the same medication at different times. If any prior or concomitant medication is classified into multiple ATC classes, the medication will be summarized separately under each of these ATC classes. The summary tables will be sorted on decreasing frequency of drug class and decreasing frequency of drug name in a given drug class. In case of equal frequency regarding drug class (respectively drug name), alphabetical order will be used. In case any specific medication does not have ATC classification level 2 coded term, it will be summarized under 'Unavailable ATC classification' category.

Summary of prior and concomitant non-drug treatments will include the number and percentage of participants by MedDRA's SOC and PT in descending order of frequency. Participants will be counted only once within an SOC or PT even if he/she received the same treatment multiple times.

6.5.5. Subsequent anticancer therapies

The following analyses will be based on the Safety Set.

Subsequent anticancer therapies are defined as medications/procedures entered in the 'Concomitant Medications' (with 'Category of Medication' = 'Follow-up Cancer Therapy'), 'Radiation Treatment' (with 'Subcategory' = 'Curative in intent'), and 'Non-drug Treatments' (with 'Category' = 'On-study Cancer Surgery' and 'Outcome of Procedure' = 'Resected' or 'Partially Resected') CRF pages. The number and percentage of participants within each category (medication therapy, radiation therapy, and surgeries) will be provided.

Medications will be coded using the WHO Drug coding dictionary and will be tabulated by preferred term in descending order of frequency.

6.6. Safety Summaries and Analyses

Summaries of safety parameters will be based on the Safety Set.

6.6.1. Laboratory Data

Laboratory results will be converted to International System of Units (Système International d'unités, SI) units which will be used for applying toxicity grades and for all summaries.

Quantitative data will be summarized using simple descriptive statistics (mean, Std Dev, median, quartiles, minimum, and maximum) of actual values and change from baseline for each nominal visit over time (ie, unscheduled assessments will be excluded). The total number of participants for change from baseline will include all participants who have both a baseline and a value at the nominal visit.

As described in Section 3.4, baseline will defined as the last assessment performed on or prior to date of the first dose of study treatment. If there are multiple assessments that meet the baseline definition on the same day without the ability to determine which was truly last, then the worst grade will be assigned as the baseline grade. Several of the CTCAE terms (including Hypo/Hypercalcemia, Chronic Kidney Disease, and Activated Partial Thromboplastin) can be derived using several laboratory tests (analytes).

Results collected as strict inequalities (eg, >10, <10) will be converted to numeric values subtracting a factor of <0.001>. Expressions of the form" ≥" or "≤" will be converted to the end point. These numeric values will be evaluated for clinically significant abnormalities, but will not be included in calculations of summary statistics.

Additionally, laboratory results will be programmatically classified according to NCI-CTCAE version 4.03 grade. Non-numerical qualifiers will not be taken into consideration in the derivation of grade (eg, hypokalemia Grade 1 and Grade 2 are only distinguished by a non-numerical qualifier and therefore Grade 2 will not be derived). In summary statistics the number and percentage of participants corresponding to grades that only include non-quantitative criteria will be displayed as a blank or NA (not assessed) rather than 0. If there is any overlap between grade criteria (eg, CTCAE grading criteria for Creatinine Increased – a value can fall into one range based on comparison to Upper Limit of Normal (ULN) and another range based on comparison to baseline), the highest (worst) grade would be assigned to that record. Grade 5 is defined in the CTCAE criteria guidance as an event with an outcome of death. Since laboratory data does not collect an outcome, Grade 5 is not used when programmatically grading laboratory data.

Grade 0 or Outside Toxicity Reference (OTR) is not defined specifically by in the CTCAE guidance. However, programmatically this is used as a category to represent those participants who did not meet any of the Grades 1 to 4 criteria. If the laboratory value is evaluable for CTCAE criteria grading (numeric value is present, valid units and ranges are present as required to allow conversion to standard units and grading), and does not qualify for any of the Grade 1-4 criteria for a given lab test, then the value is assigned as Grade 0 or OTR.

Several of the CTCAE terms (including Hypo/Hypercalcemia, Chronic Kidney Disease, and Activated Partial Thromboplastin) can be derived using several laboratory tests (analytes).

Abnormalities will be described using the worst grade by scheduled timepoint and overall. Worst case overall will be determined from scheduled and unscheduled visits. Several laboratory tests have bi-directional grading criteria defined so that both low (hypo) and high (hyper) values can be graded separately. Each criterion will be summarized separately. In the cases where a value is graded as a Grade 1, 2, 3, or 4 for one of the directions, that value will also be assigned as a Grade 0 for the opposite direction for that test. For example, a value meeting the criteria for Grade 3 Hypercalcemia will be classified as a Grade 0 Hypocalcemia. For CTCAE terms that can be derived using one of several laboratory tests, the maximum post-baseline grade for a given participant and CTCAE term will be the maximum across all possible laboratory tests.

Additional laboratory results that are not part of NCI-CTCAE will be presented according to the following categories by scheduled timepoint as well as overall: below normal limit, within normal limits, and above normal limits. In the unlikely event that for a given participant, clinically significant abnormalities are noted in both directions (eg, > ULN and < Lower Limit of Normal (LLN)), then both abnormalities are counted.

Liver function tests: Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total bilirubin (TBILI) are used to assess possible drug induced liver toxicity. The ratios of test result over the ULN will be calculated and classified for these three parameters during the on-treatment period.

Summary of liver function tests will include the following categories. The number and percentage of participants with each of the following during the on-treatment period will be summarized:

- ALT ≥3×ULN, ALT ≥5xULN, ALT ≥10×ULN, ALT ≥20×ULN;
- AST ≥3×ULN, AST ≥5xULN, AST ≥10×ULN, AST ≥20×ULN;
- (ALT or AST) ≥3×ULN, (ALT or AST) ≥5×ULN, (ALT or AST) ≥10×ULN, (ALT or AST) ≥20×ULN;
- TBILI ≥2×ULN;
- Concurrent ALT ≥3×ULN and TBILI ≥2×ULN;
- Concurrent AST ≥3×ULN and TBILI ≥2×ULN;
- Concurrent (ALT or AST) ≥3×ULN and TBILI ≥2×ULN;
- Concurrent (ALT or AST) ≥3×ULN and TBILI ≥2×ULN and ALP >2×ULN;
- Concurrent (ALT or AST) ≥3×ULN and TBILI ≥2×ULN and ALP ≤2×ULN or missing.

Concurrent measurements are those occurring on the same date.

Categories will be cumulative, ie, a participant with an elevation of AST ≥10×ULN will also appear in the categories ≥5×ULN and ≥3×ULN. Liver function elevation and possible Hy's Law cases will be summarized using frequency counts and percentages.

An evaluation of Drug-Induced Serious Hepatotoxicity (eDISH) plot will also be created, with different symbols, by graphically displaying

- Peak serum ALT(/ULN) vs peak total bilirubin (/ULN) including reference lines at ALT=3×ULN and total bilirubin=2×ULN.
- Peak serum AST(/ULN) vs peak total bilirubin (/ULN) including reference lines at AST=3×ULN and total bilirubin=2×ULN.

In addition, a listing of all TBILI, ALT, AST and ALP values for participants with a post-baseline TBILI ≥ 2×ULN, ALT≥ 3×ULN or AST ≥ 3×ULN will be provided.

6.6.2. Vital Signs

Vital sign summaries will include all vital sign assessments from the on-treatment period. All vital sign assessments will be listed, and those collected outside the on-treatment period will be flagged in the listing.

All vital sign parameters will be summarized using descriptive statistics (mean, Std Dev, median, Q1, Q3, minimum, and maximum) of actual values and change from baseline for each nominal visit over time (unscheduled assessments will be excluded). The changes computed will be the differences from baseline. The total number of participants for change from baseline will include all participants who have both a baseline value and a value at the nominal visit. Baseline will be selected as defined in Section 3.4.

The number and percent of participants in each of the following minimum and maximum blood pressure, body weight, and pulse categories will be presented:

- Maximum increase from baseline in Systolic Blood Pressure ≥40 mmHg;
- Maximum decrease from baseline in Systolic Blood Pressure ≤-60 mmHg;
- Maximum increase from baseline in Diastolic Blood Pressure ≥20 mmHg;
- Maximum decrease from baseline in Diastolic Blood Pressure >-40 and ≤-20mmHg;
- Maximum decrease from baseline in Diastolic Blood Pressure ≤-40mmHg;
- Maximum increase from baseline in Body Weight ≥10%;
- Maximum decrease from baseline in Body Weight ≤-10%;
- Maximum post-baseline Pulse Rate >130 bpm;

- Minimum pose-baseline Pulse Rate <50 bpm;
- Maximum increase from baseline in pulse rate ≥30 bpm;
- Maximum decrease from baseline in pulse rate ≤-30 bpm.

All assessments, including unscheduled assessments will be considered. A participant can be included in multiple categories if different criteria are met at different timepoints.

6.6.3. Electrocardiograms

Triplicate ECGs were required at baseline. A mean score is calculated and reported for the replicate measurements.

ECG summary will include ECG assessments at baseline. All ECG assessments will be listed, and those collected during the on-treatment period for safety evaluation will be flagged in the listing.

QT, HR, RR, PR, QRS, and QTcF will be summarized using descriptive statistics (mean, Std Dev, median, quartiles, minimum, and maximum) of actual values on baseline (see Section 3.4).

6.6.4. Performance Status

The ECOG shift from baseline to the highest score during the on-treatment period will be summarized. ECOG performance status with shift from ECOG=0 or 1 to ECOG 2 or higher will also be presented in a data listing.

6.6.5. Physical Examination

Physical examination findings will only be listed.

7. INTERIM ANALYSES

7.1. Introduction

Not applicable.

7.2. Interim Analyses and Summaries

Not applicable.

8. APPENDICES

8.1. Appendix 1. List of Abbreviations

Abbreviation	Term
AE	Adverse Event
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ATC	Anatomic Therapeutic Chemical
BOR	Best Overall Response
CI	Confidence Interval
CR	Complete Response
CRF	Case Report Form
CSR	Clinical Study Report
CT	Computerized Tomography
DI	Dose Intensity
DoR	Duration of Response
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eDISH	Evaluation of Drug-Induced Serious Hepatotoxicity
EGFR	Epidermal Growth Factor Receptor
EOS	End of Study
EOT	End of Treatment
IOTA	Investigator Overall Tumor Assessment
LPFV	Last Participant First Visit
MedDRA	Medical Dictionary for Regulatory Activities
MRI	Magnetic Resonance Imaging
N/A	Not Applicable
ND	Not Done
NE	Not Evaluable
NR	Not Reached
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
NSCLC	Non-Small Cell Lung Cancer
ORR	Overall Response Rate
OTR	Outside Toxicity Reference
PD	Progressive Disease
PR	Partial Response
PT	Preferred Term
Q1	First Quartile
Q3	Third Quartile
QTc	QT interval corrected for heart rate
QTcF	QT interval calculated using Fridericia's correction factor
RDI	Relative Dose Intensity
RECIST	Response Evaluation Criteria in Solid Tumors

Abbreviation	Term
SAP	Statistical Analysis Plan
SD	Stable Disease
SI	International System of Unit
SOC	System Organ Class
Std Dev	Standard Deviation
TBILI	Total Bilirubin
TEAE	Treatment Emergent Adverse Event
ULN	Upper Limit of Normal
WHO	World Health Organization