PROTOCOL A7471055

TREATMENT ACCESS PROTOCOL FOR PATIENTS PREVIOUSLY TREATED WITH DACOMITINIB ON A CLINICAL TRIAL IN JAPAN

STATISTICAL ANALYSIS PLAN (SAP)

Version: 2.0

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TABLE OF CONTENTS

1. AMENDMENTS FROM PREVIOUS VERSION(S) 3
2. INTRODUCTION 3
2.1. Study Design 3
2.2. Study Objectives 3
3. INTERIM ANALYSES, FINAL ANALYSES AND UNBLINDING....4
4. HYPOTHESES AND DECISION RULES 4
5. ANALYSIS SETS 4
5.1. Safety Analysis Set....4
6. STATISTICAL METHODOLOGY AND STATISTICAL ANALYSES 4
6.1. Statistical Methods 4
6.1.1. Analyses of Continuous Data 4
6.1.2. Analyses of Categorical/Binary Data 4
6.2. Statistical Analyses 4
6.2.1. Safety Analysis 4
6.2.2. Standard Analysis 5
6.2.2.1. Study Conduct and Patient Disposition....5
6.2.2.2. Baseline Characteristics 5
6.2.2.3. Treatment administration/Compliance....5

1. AMENDMENTS FROM PREVIOUS VERSION(S)

Summary of Changes

Version	Rationale	Specific Changes
1.0	Not Applicable	Not Applicable
2.0	Blinded Data Review	8.2. Statistical Analyses • Added the analysis plan to pool the data from two prior studies. 8.2.1. Safety Analysis • Added the data handling rule of AEs. 8.2.2.3. Treatment administration/Compliance • Updated the analysis plan for treatment exposure.

2. INTRODUCTION

This document describes the planned statistical analyses for protocol A7471055, dated Jan 28, 2015. This analysis plan is meant to supplement the study protocol. Any deviations from this analysis plan will be described in the Clinical Study Report.

Note: in this document any text taken directly from the protocol is ***italicised***.

2.1. Study Design

This is a multi-center, open label, treatment extension study open in Japan only. Eligible patients include those with advanced cancer who received and tolerated single-agent dacomitinib in a prior clinical study and have the potential to derive continued clinical benefit based on investigator judgment. Patients enrolled in this extension study may continue to receive dacomitinib starting at the current dose level in the prior study. Patients may continue to be treated with dacomitinib on this protocol as long as there is evidence of clinical benefit in the judgment of the investigator.

The patients will be enrolled into this extension study from the two prior studies (A7471009 and A7471050).

2.2. Study Objectives

Primary Objective:

- *To allow access to dacomitinib for patients who received dacomitinib on a prior study in Japan and who have the potential to derive continued clinical benefit from single-agent dacomitinib treatment without unacceptable toxicity based upon the investigator's judgment.*

Secondary Objective:

- *To monitor the specific long-term safety and tolerability of single-agent dacomitinib in patients who have already received dacomitinib on a prior study in Japan.*

3. INTERIM ANALYSES, FINAL ANALYSES AND UNBLINDING

Formal interim analysis is not planned. Unblinding is inapplicable to this open label study.

4. HYPOTHESES AND DECISION RULES

No statistical hypotheses and decision rules are defined.

5. ANALYSIS SETS

5.1. Safety Analysis Set

Safety analysis set is the as-treated population which will include all patients who receive any study medication.

6. STATISTICAL METHODOLOGY AND STATISTICAL ANALYSES

6.1. Statistical Methods

6.1.1. Analyses of Continuous Data

Descriptive statistics, including the mean, standard deviation, median, minimum, and maximum values, will be provided for continuous endpoints.

6.1.2. Analyses of Categorical/Binary Data

The number and percentage of patients in each category will be provided for categorical/binary variables.

6.2. Statistical Analyses

Summary tables as described below will be provided and all data collected in this study will be presented in listings. In the statistical analyses, the data of patients rolled over from study A7471009 and those from study A7471050 will be pooled.

6.2.1. Safety Analysis

AEs will be summarized by the frequency of patients experiencing treatment emergent AEs corresponding to system organ class (SOC) and preferred term (PT) according to MedDRA terminology. AEs will be graded by NCI CTCAE v4.0. AEs will be summarized by relatedness to trial treatment. The percentage of patients with an event will be calculated using the number of patients in the safety analysis set as the denominator.

AEs will not be double counted across studies (ie, prior studies and this study). Counting of AEs will be based on start date of AE. If the start date of an AE is in the prior study, the end date of the AE in this study and severity of AE remained the same in both studies or became lower, then the AE will be counted in the prior study, not in this study. However, if the same

AE started in the prior study, and get worse in severity in this study, then the AE will be counted in both studies.

Treatment emergent AEs associated with permanent discontinuation, temporary discontinuation or dose reduction will also be summarized respectively by MedDRA SOC and PT.

A summary of serious adverse events and listing of deaths reported as serious adverse events will be provided.

6.2.2. Standard Analysis

Descriptive statistics will be used to summarize study conduct, patient disposition, baseline characteristics, and treatment administration/compliance.

6.2.2.1. Study Conduct and Patient Disposition

The number of patients in safety analysis set including number and percent enrolled, treated, discontinued for study medication and assessed for AEs.

6.2.2.2. Baseline Characteristics

Demographic characteristics and medical history will be summarized in frequency tables and descriptive statistics will be provided for quantitative variables.

6.2.2.3. Treatment administration/Compliance

The following study treatment exposure summaries will be provided.

Extent of Treatment

The extent of treatment will be summarized by initial prescribed daily dose and in total as follows:

- The number and percent of patients within 26, 52, 78, 104, 156, 208, 260, >260 weeks of treatment.
- Duration of study treatment (weeks) summarized with mean, median, minimum, and maximum.

Dose Administration and Dose Intensity

- Definitions:
  - A **dose reduction** is defined as actual dose taken is at least 33% less than the prescribed dose taken on any given day for any reason with the exception of a day with total dose administered of 0mg, which is not considered a dose reduction.
  - A **dose interruptions/missed dose** is defined as a dosing interval of any duration with daily dose of 0 mg.

- Number (%) of patients with dose reduction/interruption will be summarized by initial prescribed daily dose and in total.

Tables will be provided by initial prescribed daily dose whenever applicable for:

- Dose received/Cumulative dose.

- Relative dose (ie, percent of actual total dose received relative to intended total dose initially planned per protocol, where actual total dose = total dose received as recorded on CRF; intended total dose = (prescribed daily dose at beginning of the study)*(actual dose duration)).

Follow-up Therapy

A listing for follow-up cancer therapy will be provided with subject, regimen, date of last dose of study treatment, start date of subsequent cancer regimen, time from last dose of study drug to the first subsequent regimen, drugs administered, end date of subsequent cancer regimen, duration of the subsequent regimen.