NOVARTIS

Clinical Development

BKM120

BKM120Z2402 / NCT01693614

An open-label phase II study of BKM120 in patients with relapsed and refractory diffuse large B-cell lymphoma, mantle cell lymphoma and follicular lymphoma

Statistical Analysis Plan (SAP)

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List of abbreviations

AE	Adverse event
CSR	Clinical Study report
DLBCL	Diffuse large B-cell lymphoma
FL	Follicular lymphoma
MCL	Mantle cell lymphoma
NCI	National Cancer Institute
OS	Overall Survival
PFS	Progression-Free Survival
RAP	Report and Analysis Process
SAP	Statistical Analysis Plan
SOC	System Organ Class
TFLs	Tables, Figures, Listings

1 Introduction

This statistical analysis plan (SAP) describes all planned analyses for the final clinical study report (CSR) of study CBKM120Z2402, an open-label, phase II study of BKM120 in patients with relapsed and refractory diffuse large B-cell lymphoma, mantle cell lymphoma and follicular lymphoma.

The content of this SAP is based on protocol CBKM120Z2402 Amendment version 4.0. All decisions regarding final analysis, as defined in the SAP document, have been made prior to database lock.

The final CSR for this study will be the short close out CSR. Thus, only outputs outlined in the short close out CSR guidelines (version 2.0 dated 20-Jan-2017) will be generated. For this study the primary CSR was done based on interim lock (cut-off date 25-Feb-2015). This SAP document will contain details regarding outputs which were not part of the primary CSR and rest of the analysis will be referred to primary CSR SAP and TFL shells.

Please refer to Primary CSR SAP (RAP M3) and TFL shells (RAP M7) for study design, study objectives and endpoints.

2 Statistical methods

2.1.1 Primary CSR RAP M3 and M7

For the final analysis, please refer to the RAP module 3 in CREDI in the following path.

[redacted]

For the final analysis, please refer to the RAP module 7 in CREDI in the following path.

[redacted]

2.1.2 Clinical Trial Safety Disclosure

For the legal requirements of ClinicalTrials.gov and EudraCT, two required tables on treatment emergent adverse events which are not serious adverse events with an incidence greater than 5% and on treatment emergent serious adverse events and SAE suspected to be related to study treatment will be provided by system organ class and preferred term on the safety set population.

If for a same patient, several consecutive AEs (irrespective of study treatment causality, seriousness and severity) occurred with the same SOC and PT:

- a single occurrence will be counted if there is ≤ 1 day gap between the end date of the preceding AE and the start date of the consecutive AE
- more than one occurrence will be counted if there is > 1 day gap between the end date of the preceding AE and the start date of the consecutive AE

For occurrence, the presence of at least one SAE / SAE suspected to be related to study treatment / non SAE has to be checked in a block e.g., among AE's in a ≤ 1 day gap block, if at least one SAE is occurring, then one occurrence is calculated for that SAE.

The number of deaths resulting from SAEs suspected to be related to study treatment and SAEs irrespective of study treatment relationship will be provided by SOC and PT.

2.1.3 List of outputs for final CSR

Below outputs will be generated for final CSR as per short close out CSR guidelines.

- In-text tables:

Table 10- 1 Patient disposition by cohort (Full analysis set)

Table 11- 2 Demographic characteristics, by cohort (Full analysis set)

Table 11- 9 Analysis of PFS based on investigator assessment using Kaplan-Meier method by cohort (Full analysis set)

Table 11- 11 Analysis of OS using Kaplan-Meier method (Full analysis set)

Table 12- 1 Duration of exposure to study drug by cohort (Safety set)

Table 12- 5 Adverse events, regardless of study drug relationship, by cohort, by primary system organ and maximum grade (Safety set)

Table 12- 6 Adverse events regardless of study drug relationship, by cohort, by preferred term and maximum grade (>=5% in any cohort) (Safety set)

Table 12- 7 Adverse events suspected to be study drug related, by cohort, by preferred term and maximum grade (>=5% in any cohort) (Safety set)

Table 12- 9 Serious adverse events, regardless of study drug relationship, by cohort, primary system organ class, preferred term and maximum grade (Safety set)

Table 12-10 Adverse events leading to study drug discontinuation, by cohort, regardless of study drug relationship, by primary system organ class, preferred term and maximum grade (Safety set)

- Post-text tables, figures and listings :

Table 14.1-1.1 Patient disposition by cohort (Full analysis set)

Table 14.1-4.1 Demographic characteristics, by cohort (Full analysis set)

Figure 14.2-1.7 Kaplan-Meier plot of overall survival- DLBCL (Full analysis set)

Figure 14.2-1.8 Kaplan-Meier plot of overall survival - MCL (Full analysis set)

Figure 14.2-1.9 Kaplan-Meier plot of overall survival - FL (Full analysis set)

Table 14.2-2.4 Analysis of PFS based on investigator assessment using Kaplan-Meier method (Full analysis set)

Table 14.2-2.6 Analysis of OS using Kaplan-Meier method (Full analysis set)

Table 14.3-1.1 Duration of exposure to study drug by cohort (Safety set)

Table 14.3.1-1.1 Adverse events, regardless of study drug relationship, by cohort, primary system organ class, preferred term and maximum grade (Safety set)

Table 14.3.1-1.3 Deaths, by primary system organ class, preferred term and cohort (Safety set)

Table 14.3.1-1.4 Adverse events, suspected to be study drug related, by cohort, by primary system organ class, preferred term and maximum grade (Safety set)

Table 14.3.1-1.6 Serious adverse events, regardless of study drug relationship, by cohort, primary system organ class, preferred term and maximum grade (Safety set)

Table 14.3.1-1.9 Adverse events leading to study drug discontinuation, by cohort, regardless of study drug relationship, by primary system organ class, preferred term and maximum grade (Safety set)

Table 14.3.1-1.13 Clinically notable adverse events (Safety set)

Table 14.3.1-1.15 On-treatment deaths and serious adverse events (related) by system organ class and preferred term (Safety set)

Table 14.3.1-1.16 On-treatment non-serious adverse events (threshold>=5%) by system organ class and preferred term (Safety set)

Listing 14.3.2-1.1 Deaths during treatment by cohort (Safety set)

Listing 14.3.2-1.6 Adverse events by specific safety event categories by cohort (Safety set)

Listing 16.2.1-1.1 Treatment and study completion by cohort (Full analysis set)

Listing 16.2.4-1.1 Patient baseline demographics by cohort (Full analysis set)

Listing 16.2.5-1.1 Dose administration record by cohort (Safety set)

Listing 16.2.6-1.8 Progression free survival (PFS) as per investigator by cohort (Full analysis set)

Listing 16.2.6-1.10 Overall Survival by cohort (Full analysis set)

Listing 16.2.7-1.1 Adverse events by cohort (Safety set)

3 Reference

Guidelines for short close out CSR, version 2.0 dated 20-Jan-2017