Statistical Analysis Plan

A Multicenter Open-Label, Phase 1b/2 Study of the Bruton's Tyrosine Kinase (BTK) Inhibitor, Ibrutinib, in Combination with Lenalidomide and Rituximab in Subjects with Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Protocol PCYC-1123-CA; Phase 1b/2

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LIST OF ABBREVIATIONS

ABC	activated B-cell like (DLBCL subtype as determined by GEP)
AE	adverse event
ANC	absolute neutrophil count
BTK	Bruton's tyrosine kinase
CFR	Code of Federal Regulations
CI	confidence interval
CR	complete response
CT	computed tomography
CYP	cytochrome P
DLBCL	diffuse large B cell lymphoma
DLT	dose limiting toxicity
DOR	duration of response
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
EDC	electronic data capture
eCRF	electronic case report form
FDA	Food and Drug Administration
GCB	germinal-cell B-cell-like (subtype)
GEP	gene expression profiling
IV	intravenous
MAD	maximum administered dose
MedDRA	Medical Dictionary for Regulatory Activities
MTD	maximum tolerated dose
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
NHL	non-Hodgkin's lymphoma
ORR	overall response rate
OS	overall survival
PCYC	Pharmacyclics Inc. (Sponsor)
PD	progressive disease
PFS	progression-free survival
PK	pharmacokinetic(s)
PO	per os (oral)
PR	partial response

RP2D	Recommended Phase 2 Dose
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	stable disease
SPD	sum of the product of the diameters

1 INTRODUCTION

This statistical analysis plan (SAP) is based on Protocol Amendment 5, dated on 01JUN2016, and is to define key elements including variable definitions, and statistical methods for analysis of data in the evaluation of efficacy and safety of the study PCYC-1123-CA. Analyses of biomarker and pharmacokinetics data will be addressed in separate documents.

Analysis methods specified in this document take precedence over those described in the protocol, should there be any difference.

1.1 Study Design

This Phase 1b/2 study is designed to assess the safety and efficacy of ibrutinib in combination with lenalidomide and rituximab in subjects with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) ineligible for a stem cell transplant. Phase 2 will evaluate only subjects with the non-GCB subtype of de novo DLBCL. Approximately 46 subjects will be enrolled in the Phase 1b portion. Phase 2 will enroll approximately 55 subjects to ensure enrollment of at least 49 response-evaluable subjects at 20 mg lenalidomide; approximately 28 additional subjects may be enrolled at 25 mg lenalidomide.

1.1.1 Phase 1b

In the dose escalation portion of the study, up to four cohorts may be explored, and the lenalidomide dose escalation will follow the 3+3+3 principle for the maximum tolerated dose (MTD) determination. Due to the fact that the subject population studied is significantly ill, and an inability to complete the dose-limiting toxicity (DLT) observation period may occur due to progression of disease, additional subjects may be screened and enrolled in each cohort. The DLT rules will continue to apply whereas if 1 DLT is observed, the cohort will be expanded to 6, and if 2 DLTs occur, the cohort will be expanded to 9.

Ibrutinib will be administered orally once daily at 560 mg and will be initiated on Day 1 of the first cycle. Treatment will be continuous (without interruption) and will continue until disease progression or unacceptable toxicity. Lenalidomide will be administered orally once daily at the dose designated by cohort on Days 1-21 of each 28-day cycle and will continue until disease progression or unacceptable toxicity. Rituximab 375 mg/m^2 will be administered intravenously (IV) on Day 1 of each 28-day (4-week) cycle for 6 cycles.

If 3 subjects in Cohort 1 experience a DLT, dose level -1 was planned to be enrolled (Table 1). After completion of Cohort 1, due to 3 DLTs in 7 evaluable subjects, a cohort at Dose Level -1 was opened. After completion of the Dose Level -1 cohort, if <33% of subjects experience a DLT, dose re-escalation to higher dose levels starting with the

lenalidomide dose of 15 mg may occur. If the dose level of 20 mg lenalidomide is determined to be safe and tolerated in the Phase 1b, this dose will be considered the recommended Phase 2 dose (RP2D), and a Phase 2 cohort with 20 mg lenalidomide will be initiated. Concurrent with the Phase 2 at 20 mg lenalidomide, a Phase 1b cohort with 25 mg lenalidomide may be initiated. If the interim analysis of the 20 mg lenalidomide cohort is negative, the 25 mg lenalidomide dose may be used in an additional cohort in the Phase 2, if safe and tolerated in the Phase 1b.

Table 1: Phase 1b Dose Levels

28-Day Dosing Cycle	Ibrutinib[a]	Lenalidomide[b]	Rituximab[c]
Dose Level -1[d]	560 mg once daily	10 mg	375 mg/m^2
Dose Level 1 = starting dose (Cohort 1 & 1+)	560 mg once daily	15 mg	375 mg/m^2
Dose Level 2 (Cohort 2)	560 mg once daily	20 mg	375 mg/m^2
Dose Level 3 (Cohort 3)	560 mg once daily	25 mg	375 mg/m^2

a. Ibrutinib will be administered orally once daily beginning Cycle 1 Day 1
b. Lenalidomide will be administered orally once daily on Days 1-21 of each 28-day cycle
c. Rituximab will be administered IV on Day 1 of each 28-day cycle for 6 cycles
d. If <33% of subjects experience a DLT at Dose Level -1, dose re-escalation to a higher dose level may occur.

At least 6 subjects will be treated at the MTD or in any cohort defined as the RP2D that supports the Phase 2.

1.1.2 Phase 2

The Phase 2 part of this study will be conducted as an international, multicenter, open-label study. Phase 2 will enroll approximately 49 response-evaluable subjects at 20 mg lenalidomide; approximately 28 additional subjects may be enrolled at 25 mg lenalidomide.

Eligible subjects will receive ibrutinib, lenalidomide and rituximab per the treatment schedule as shown below (Table 2). If determined to be safe and tolerated in the Phase 1b portion of the trial, the proposed dose of lenalidomide for Phase 2 is 20 mg. Subjects will be treated until disease progression or unacceptable toxicity.

Table 2: Treatment Schedule[a]

	Cycles 1-6	Cycles 7+
Ibrutinib	PO daily	PO daily
Lenalidomide	PO daily Days 1-21	PO daily Days 1-21
Rituximab	IV on Day 1	NA

[a] Each cycle will be 28-days in length (4 weeks) and subjects will continue until disease progression or unacceptable toxicity. Rituximab will be given for the first 6 cycles.

An interim analysis might be performed including approximately 28 evaluable subjects with adequate tumor response assessments. Details of the interim analysis and decision rules will be described in Section 1.5. In addition, if there are safety concerns, a cohort with ibrutinib and lenalidomide without rituximab may be considered in the Phase 2 part of the study.

Immunohistochemistry (IHC) and gene expression profiling (GEP) will be used to assess subject status with respect to the subtype of DLBCL. The limitations of IHC allow only a distinction between subjects as either non-germinal center B cell-like (non-GCB) or GCB phenotype, since within the non-GCB group, one may include subjects with a true unclassified (intermediate) subtype. With GEP, the subjects can be further categorized into the following subtypes: ABC, GCB, unclassified, and unknown due to tissue limitations. Throughout the protocol, the description of enrolled subjects as non-GCB is based on IHC testing used at screening; and the use of the term ABC subtype refers to subjects who have been subsequently profiled by GEP and then classified as the true ABC subtype.

1.2 Endpoints

1.2.1 Phase 1b

Primary Endpoints:

- MTD or RP2D
- Safety and tolerability of ibrutinib in combination with lenalidomide and rituximab in subjects with relapsed or refractory DLBCL

Secondary Endpoints:

- Overall response rate (ORR) and complete response (CR) rate

1.2.2 Phase 2

Primary Endpoint:

- ORR

Secondary Endpoints:

Efficacy:

- CR rate
- Duration of response (DOR)
- Progression-free survival (PFS)
- Overall survival (OS)

Safety:

- Frequency, severity, and relationship (to study drug) of AEs
- Frequency of AEs requiring discontinuation of study drug or dose reductions

Exploratory Analyses:

- Efficacy endpoints by DLBCL subtype per GEP
- Change in peripheral T/B/NK counts
- Change in serum immunoglobulin levels (IgG, IgM, and IgA)

1.3 Statistical Hypotheses

The main analysis for the Phase 2 part of this study will be the comparison of the response rate to the ORR of a historical control of 40%. The null hypothesis that the true ORR is 40% will be tested against a one-sided alternative that the ORR is 60%.

1.4 Sample Size Determination

The planned sample size for the Phase 2 part of this study is approximately 55 subjects to ensure enrollment of at least 49 response-evaluable subjects at 20 mg lenalidomide.

An interim analysis might be performed including approximately 28 evaluable subjects with adequate tumor response assessments. If only 11 or fewer responders (≤11/28) are observed, the Sponsor may consider discontinuation of the study; however, if there is evidence for clinical benefit from biomarker data or tumor measurements (showing clinically relevant tumor reductions, e.g. 40%, that fit the criteria for the response of SD), continued enrollment may be supported.

The main analysis will be the comparison of the response rate to the ORR of a historical control of 40%. The null hypothesis that the true ORR is 40% will be tested against a one-sided alternative that the ORR is 60%. The null hypothesis will be rejected if 27 or more responses are observed in the 49 subjects.

This design yields a 1-sided type I error rate of 0.025 and power of 80% when the true ORR is 60%. This statistical design including the number of subjects and the number of responders follows the statistical framework of Simon's minimax two-stage design (Simon 1989). Enrollment will continue while the interim analysis is being performed.

Approximately 28 additional subjects may be enrolled at 25 mg lenalidomide to explore the efficacy and safety at this higher dose of lenalidomide in Phase 2.

1.5 Planned Analyses

1.5.1 Timing of Analyses

An analysis will occur approximately 12 months after the last subject initiates study treatment or when all subjects have discontinued from the study treatment, whichever occurs first. A final analysis will occur 2 years after the last subject has been enrolled and will be reported in the CSR. The study completion is defined as 3 years from the last study treatment, the time point all subjects have exited the study due to any reason, or study termination at the Sponsor's discretion, whichever occurs first.

1.5.2 Interim Analysis

An interim analysis for Phase 2 at the 20 mg lenalidomide dose might be performed including approximately 28 evaluable subjects with adequate tumor response assessment. If only 11 or fewer responders ($\leq$ 11/28) are observed, the Sponsor may consider discontinuation of the study; however, if there is evidence for clinical benefit from biomarker data or tumor measurements (showing clinically relevant tumor reductions, e.g. 40%, that fit the criteria for SD), continued enrollment may be supported.

At the interim analysis, the review committee could recommend:

- Continuation or discontinuation of the study with 20 mg lenalidomide; or
- Increase of the lenalidomide dose to 25 mg, if determined to be safe and tolerated in the Phase 1b, including approximately 28 evaluable subjects with adequate tumor response assessment followed by an interim analysis.

In addition, if there are safety concerns, a cohort with ibrutinib and lenalidomide without rituximab may be considered in the Phase 2. The decisions based on the interim analysis will be made by the Sponsor (at a minimum: the Medical Monitor or designee, a Drug Safety representative and a Biostatistician). Enrollment in the 20 mg lenalidomide cohort will continue while the interim analysis is being performed.

1.6 Testing Procedure and Level of Significance

The null hypothesis that the true ORR is 40% will be tested at a 2-sided alpha of 0.05 for Part 2 at the 20 mg lenalidomide dose. If the lower bound of the 95% CI is greater than 40%, the study will be claimed as positive for Part 2 at the 20 mg lenalidomide dose.

1.7 Blinding and Randomization Methods (if applicable)

1.7.1 Blinding Method

This is an open-label study. Blinding does not apply.

1.7.2 Randomization Method

This is not a randomized study. Subjects are enrolled according to the order of Phase 1b to Phase 2 and low dose to high dose cohorts. Note: The Phase 2 was started at a 20 mg lenalidomide dose while the Phase 1b was still ongoing with a 25 mg lenalidomide cohort.

2 GENERAL ANALYSIS CONSIDERATION

The Phase 1b part of this study is a dose escalation study. All safety and efficacy assessments will be summarized by dose group. The Phase 2 part of this study is designed to assess the efficacy and safety of ibrutinib in combination with lenalidomide and rituximab in subjects with relapsed or refractory de novo non-GCB DLBCL.

In general, continuous variables will be summarized with descriptive statistics (mean, standard error or standard deviation, median, quartiles, minimum, and maximum). For categorical variables, the number and percentage of subjects in each applicable category will be provided. Time-to-event or duration-of-event endpoints will be based on the event and censoring dates.

All statistical analyses will be performed using SAS® version 9.3 or higher.

2.1 Analysis Sets

All-treated analysis population (Phase 1b/2)

The all-treated analysis population will include subjects who have been enrolled in the study and received any dose of study drug(s) in each study phase, respectively. This is the primary analysis population for all efficacy endpoints (i.e., PFS, OS), except ORR and the CR rate for the Phase 1b and Phase 2. This is also the sensitivity analysis population for ORR and CR.

Response-evaluable Population (Phase 1b/2)

The response-evaluable population in the Phase 1b/2 study is defined as subjects in the all-treated population who have measurable disease at baseline and have at least 1 adequate post-treatment disease assessment by the investigator before the start of a subsequent anti-cancer therapy. This is the primary analysis population for ORR and the CR rate.

Safety Population (Phase 1b/2)

The safety population consists of all enrolled subjects who received at least one dose of study drug. The safety population will be used for the analysis of all safety and dosing data. For this study, this population is equivalent to the all-treated analysis population. They are interchangeably used.

2.2 Definitions of Subgroups

Analyses for the baseline subgroups (hereafter referred as "subgroup" or "subgroups") will be performed for the selected primary and secondary endpoint variables analyses for Phases 1a and 2 except where noted in Table 3.

Table 3: Baseline Subgroups

Baseliner Characteristics	Subgroup	Analysis Type
DLBCL subtype by GEP	ABC, GCB and Unclassified	**E**
DBLC subtype by IHC	GCB and Non-GCB	**E**
Transformed DLBCL (Phase 1b only)	Yes	E
Subjects with refractory disease	Yes	ORR and Baseline
Subjects with relapsed disease	Yes	ORR and Baseline
Subjects with primary refractory disease	Yes	ORR and Baseline

Analysis type: E = Efficacy (ORR, CR, PFS and OS).

3 SUBJECT INFORMATION

3.1 Subject disposition

Subject enrollment will be summarized by dose cohort in Phase 1b and in Phase 2, respectively. The disposition of all enrolled subjects will be summarized by study phase.

The disposition tables will include the following summaries.

- Analysis population (all-treated subjects)
- Enrollment by region, country and investigator
- Study treatment disposition and discontinuation
- Study status and the time on study

The Kaplan-Meier estimates will be calculated to estimate the time on study using reversed censoring from the OS analysis.

3.2 Demographics and Baseline characteristics

Subject demographics (including age, sex, and race/ethnicity), general baseline characteristics (including ECOG performance status, weight and height), and baseline disease characteristics (including Ann Arbor staging, bulky disease, DLBCL category and number of prior therapies) will be summarized. Summary statistics will include means, standard deviations, and medians for continuous variables and proportions for categorical variables.

Concordance is summarized for the all-treated population between the DLBCL subtypes per GEP test by central lab and per IHC test by local lab.

3.3 Prior, Concomitant, and Subsequent Medications/Procedures

Medications will be coded to preferred term and Anatomical Therapeutic Chemical (ATC) class according to World Health Organization (WHO) Drug dictionary.

Prior medications are defined as medications that started prior to the first dose date of study drug. Prior anti-neoplastic therapies will be summarized separately.

Concomitant medications are defined as medications that were taken at any time on treatment (i.e. from the date of the first dose of study drug through the date of the last dose of study drug) and will be summarized separately. Concomitant use of CYP3A inhibitors (strong, moderate, and weak) and CYP3A4 inducers will be listed and summarized separately.

3.4 Subsequent Anti-Cancer Treatment

Subsequent anticancer therapies are anti-DLBCL treatments that started after discontinuation of study treatment (i.e. started after the last dose of study drug) will be summarized for the all-treated population by type (e.g. radiotherapy, systemic therapy, bone marrow or stem cell transplant).

3.5 Extent of Exposure to Study Drug

For each study treatment, the number of treatment cycles each subject received will be summarized for the all-treated population. Subjects with any dose interruption or dose reduction due to AEs will be summarized.

Summary tables for ibrutinib, lenalidomide, and rituximab will present duration of treatment, the number of doses received, the total amount of study drug received, the average dose per

administration, the relative dose intensity, and subjects with at least 1 dose modification (interruption or reduction) due to AE.

For rituximab, the average dose per administration, relative dose intensity, the number and percentage of subjects with infusion interruption, duration of interruption, and at least 1 dose modification will be summarized.

4 EFFICACY EVALUATIONS

The Response-evaluable population (Phase 1b/2) is the primary analysis population for ORR and the CR rate. The ORR and the CR rate will be calculated for the all-treated population as well. The all-treated population is the primary analysis population for all other efficacy endpoints (i.e. PFS, OS). The analysis of endpoints is presented in Table 4.

The scanned images will be centrally stored for a possible future independent review of overall response. In case PCYC decides to implement an independent review of tumor response data, the overall response as assessed independently will become the primary analysis set for ORR, CR, DOR and PFS, and the previous analyses by investigators' assessments will become a secondary analysis set.

Table 4: Definitions and Analyses for Efficacy Endpoints

Endpoint	Definition	Analysis Method
Phase 1b:		
Secondary Endpoints (for all subtypes of DLBCL):		
ORR	The ORR is defined as the rate of subjects who achieve either a PR or CR, according to the revised International Working Group Response Criteria for NHL (Cheson 2007), as assessed by the Investigator.	ORR and its corresponding exact binomial 2-sided 95% CI, based on the response-evaluable population enrolled in Phase 1b. <u>Sensitivity</u> Analysis based on the all-treated population enrolled in Phase 1b. In addition, waterfall plot for maximum percent reduction in tumor size and time to response will be summarized.
CR rate	The ORR is defined as the rate of subjects who achieve a CR, according to the revised International Working Group Response Criteria for NHL (Cheson 2007), as assessed by the Investigator.	The same as for ORR

Endpoint	Definition	Analysis Method
Phase 2:		
Primary Endpoint:		
ORR	The ORR is defined as the rate of subjects who achieve either a PR or CR, according to the revised International Working Group Response Criteria for NHL (Cheson 2014), as assessed by the Investigator.	ORR and its corresponding exact binomial 2-sided 95% CI, based on the response-evaluable population enrolled in Phase 2. Sensitivity Analysis based on all-treated population enrolled in Phase 2. In addition, a waterfall plot for maximum percent reduction in tumor size and time to response will be summarized.
Secondary Endpoints:		
CR rate	The ORR is defined as the rate of subjects who achieve a CR, according to the revised International Working Group Response Criteria for NHL (Cheson 2014), as assessed by the Investigator	The same as for ORR
DOR	Time from the date of the first documented response (CR or PR) to the first documented evidence of PD or death from any cause. For subjects who have achieved an overall response but did not die or progress at the time of analysis, DOR will be censored on the date of the last adequate post-baseline disease assessment, or on the date of the first occurrence of response (CR or PR) if there is no disease assessment afterwards.	Analysis of DOR will be based on the subjects who have achieved a response (CR or PR) prior to initiation of the next line of anticancer therapy in the all-treated population enrolled in Phase 2. The median DOR and its 2-sided 95% CI will be obtained using the same method described for PFS. Similar analysis for duration of CR, as defined as time from the date of the initial CR to the first documented evidence of PD or death from any cause, will be performed for all treated subjects who have achieved a response of CR prior to initiation of the next line of anticancer therapy in Phase 2.
PFS	Time from the date of the first dose of study drug to confirmed PD or death from any cause, whichever occurred first. For subjects without disease progression or death, PFS data will	Kaplan-Meier method based on the all-treated population by dose level enrolled in Phase 2. The median PFS and its 2-sided 95% CI will be provided. PFS at landmark time points (e.g., 3, 6, 9, 12 months from the first study drug dose date) will also be obtained by the Kaplan-Meier method; 95% CI for the landmark PFS rates will be calculated.

Endpoint	Definition	Analysis Method
	be censored at the date of the last tumor assessment.	
OS	Overall survival (OS) is defined as the time from the date of the first dose of study drug to the date of death due to any cause. For subjects who are not known to have died at or prior to the database lock date, OS data will be censored at the date last known alive. Subjects who withdraw consent prior to study closure will be censored on the date of the consent withdrawal.	Kaplan-Meier method based on the all-treated population by dose level enrolled in Phase 2. The median OS and its 2-sided 95% CI will be provided. OS at landmark time points (e.g., 3, 6, 9, 12 months from the first study drug dose date) will also be obtained by the Kaplan-Meier method; 95% CI for the landmark OS rates will be calculated.
Exploratory Analysis:		
Peripheral T/B/NK counts	The absolute cell counts on peripheral T/B/NK	Summary statistics will be calculated for the measured values and for their changes from baseline at each scheduled visit of assessment.
Serum immunoglobulin levels	The serum immunoglobulin levels (IgG, IgM, and IgA)	Summary statistics will be calculated for the measured values and for their changes from baseline at each scheduled visit of assessment.
Efficacy endpoints (DOR, PFS, and OS) by DLBCL subtype per GEP	See definitions above for DOR, PFS, and OS	Subgroup analyses will be performed as defined in Table 3. See analysis methods above for DOR, PFS, and OS.

ABC: Activated B cell-like; CI: confidence interval; CR: complete response; DLBCL: diffuse large B-cell lymphoma; ECOG PS: Eastern Cooperative Oncology Group Performance Status; GCB: germinal center B cell-like; GEP: gene expression profile; IHC: immunohistochemistry; KM: Kaplan-Meier; ORR: overall response rate; OS: overall survival; PD: progressive disease; PFS: progression-free survival; PR: partial response; RP2D: recommended phase 2 dose.

5 SAFETY EVALUATION

Safety data for the all-treated population will be summarized for Phase 1b by the dose for Phase 2, unless otherwise indicated. Table 5 summarizes the safety analyses to be conducted.

Adverse events will be coded in accordance with the Medical Dictionary for Regulatory Activities (MedDRA). Severity of AEs will be graded by the investigator according the NCI Common Terminology Criteria for Adverse Events (NCI-CTCAE) (version 22.1 or higher).

In general, the treatment-emergent period is defined as the period from the date of the first dose of study treatment up to 30 days after the date of the last dose of study treatment or the day before initiation of subsequent anticancer therapy, whichever comes first. Treatment-emergent AEs are those events that occur or worsen during the treatment-emergent period or that are related to the study treatment or events with a complete missing onset date but with a resolution date during the treatment phase.

All laboratory values will be converted to and reported as international standard (SI) units. In general, only data from the central laboratory will be summarized and analyzed. Laboratory parameters will be graded using the NCI CTCAE (version 4.03 or higher). Unless otherwise specified, only baseline and post-baseline values collected during the treatment-emergent period will be included in the safety analysis.

Table 5: Summary of Safety Assessments

Assessment Type	Definition	Analysis Methods
AE	TEAEs, SAEs, grade 3 or higher TEAEs, study treatment-related TEAEs, TEAEs as the primary reason for treatment discontinuation, TEAEs leading to treatment discontinuation, TEAEs leading to dose reduction, TEAEs leading to death, protocol-defined events of special interest and other safety observations	Descriptive summary statistics and/or listings
Lab	Worst post-baseline toxicity grade for selected CTCAE gradable hematology and chemistry. Abnormalities in creatinine clearance, uric acid, and liver function.	Descriptive summary statistics and/or listings. For gradable lab results, the worst toxicity grade during the study will be tabulated and the summary of treatment-emergent abnormal laboratory results with 2 or more grade worsening will be provided.
Vital Signs and other Observations Related to Safety	SBP, DBP, heart rate, body temperature, weight, and ECOG PS	The baseline and the change from baseline will be summarized by scheduled visits.
DLT	DLT	Listing

CTCAE= Common Terminology Criteria for Adverse Events; DLT: dose limiting toxicity; ECOG: Eastern Cooperative Oncology Group; TEAE: treatment-emergent adverse event; SAE= serious adverse event; SBP: systolic blood pressure; DBP: diastolic blood pressure

6 CHANGES IN PROTOCOL PLANNED ANALYSIS

Per protocol, an analysis will occur approximately 12 months after the last subject initiates study treatment or when all subjects have discontinued from the study treatment, whichever occurs first, and will be reported in the Clinical Study Report (CSR). Since the study results were summarized and presented at the American Society of Hematology Annual Meeting 2019, which was close to the time for that planned analysis, a decision was made to delay the clinical study report, which will be prepared at the final follow-up analysis, which will occur 24 months or 2 years after the last subject has been enrolled.

7 REFERENCES

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