DISCLOSURE

REDACTED STATISTICAL ANALYSIS PLAN

CC-4047-BRN-001

A PHASE 2 CLINICAL STUDY OF POMALIDOMIDE (CC-4047) MONOTHERAPY FOR CHILDREN AND YOUNG ADULTS WITH RECURRENT OR PROGRESSIVE PRIMARY BRAIN TUMORS

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STATISTICAL ANALYSIS PLAN

A PHASE 2 CLINICAL STUDY OF POMALIDOMIDE (CC-4047) MONOTHERAPY FOR CHILDREN AND YOUNG ADULTS WITH RECURRENT OR PROGRESSIVE PRIMARY BRAIN TUMORS

INVESTIGATIONAL PRODUCT (IP): **POMALIDOMIDE**
PROTOCOL NUMBER: **CC-4047-BRN-001**
AMENDMENT #3.0 DATE FINAL: **20 DECEMBER 2017**

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SIGNATURE PAGE

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INVESTIGATIONAL PRODUCT	POMALIDOMIDE
PROTOCOL NUMBER	CC-4047-BRN-001
PROTOCOL VERSION, DATE	Amendment #3.0, 20 December 2017
SIGNATURE STATEMENT	By my signature, I indicate I have reviewed this SAP and find its contents to be acceptable.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1. LIST OF ABBREVIATIONS

Table 1: Abbreviations and Specialist Terms

Abbreviation or Specialist Term	Explanation
AE	Adverse event
AESI	Adverse event of special interest
ALT (SGPT)	Alanine aminotransferase
ANC	Absolute neutrophils count
AST (SGOT)	Aspartate amino transferase
ATC	Anatomical therapeutic chemical
BLQ	Below the limit of quantitation
BSA	Body surface area
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
CNS	Central nervous system
CR	Complete response
CRP	Clinical Research Physician
CSR	Clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
CV	Coefficient of variation
DBP	Diastolic blood pressure
DIPG	Diffuse intrinsic pontine glioma
DMC	Data monitoring committee
DoR	Duration of response
eCRF	Electronic case report form
FCBP	Female of child bearing potential
FCCBP	Female children of childbearing potential
GCP	Good Clinical Practice

Abbreviation or Specialist Term	Explanation
IAF	Informed assent form
ICH	International Council for Harmonisation
ICF	Informed consent form
ITT	Intent-to-treat
IVRS	Interactive voice recognition system
Max	Maximum
MedDRA	Medical Dictionary for Regulatory Activities
Min	Minimum
MRI	Magnetic resonance imaging
NCI	National Cancer Institute
OR	Objective response
ORR	Objective response rate
ORSDR	Objective response and long-term SD rate
OS	Overall survival
PD	Progressive disease
PDI	Planned dose intensity
PFS	Progression-free survival
PK	Pharmacokinetic
PR	Partial response
PT	Preferred term
Q1	First quartile
Q3	Third quartile
SAP	Statistical analysis plan
SAS	Statistical Analysis Systems
SBP	Systolic blood pressure
SD	Stable disease
SAE	Serious adverse event

Abbreviation or Specialist Term	Explanation
SMQ	Standardized MedDRA queries
SOC	System organ class
SPM	Second primary malignancies
SQRT	Square root of time
StdDev	Standard deviation
TEAE	Treatment-emergent adverse event
TEN	Toxic epidermal necrolysis
TLG	Tables, listings, and graphs
Vss	Volume of distribution at steady state
WBC	White blood cells
WHO	World Health Organization
WHODD	World Health Organization Drug Dictionary
V	Variance of the log-transformed values

2. INTRODUCTION

This statistical analysis plan (SAP) describes the analyses and data presentations for Celgene's protocol CC-4047-BRN-001 "A Phase 2 clinical study of pomalidomide (CC-4047) monotherapy for children and young adults with recurrent or progressive primary brain tumors", Amendment #3.0, dated 20 December 2017. This study was set up with the objective of evaluating the efficacy of pomalidomide as monotherapy in recurrent or progressive specific primary brain tumors in pediatric subjects and young adults with regards to response and long-term stable disease (SD). In addition, further evaluation of anticancer activity will be established and the safety profile identified. Evaluation of pharmacokinetic (PK) data in the study disease populations will also be performed. This SAP contains definitions of analysis populations, derived variables, and statistical methods for the analysis of all efficacy, safety, and PK endpoints.

There are four primary brain tumor types being studied: high-grade glioma, medulloblastoma, ependymoma, and diffuse intrinsic pontine glioma (DIPG). Each tumor type/disease indication, will form a single study arm with each of these study arms being run in parallel to each other. A Simon's Optimal Two-stage study design will be applied to each tumor type/disease indication. In stage one, a total of up to 9 evaluable subjects for the primary endpoint will be enrolled in each arm and treated with up to an additional further 11 in stage two. In total, up to 80 subjects evaluable for the primary endpoint are expected to be enrolled into this study.

Furthermore, the purpose of this SAP is to specify, prior to database lock, the statistical approaches for all analyses to be performed during the life time of this study including the interim analyses, the complete and final analysis of study data for purpose of the clinical study report (CSR) and analysis to be conducted at the close of the study. This SAP will be finalized and signed prior to the clinical database lock for the final primary analysis which will be used for the CSR, for which the cut-off date will be set to the last subject's 28-Day Post Treatment Safety Follow-up visit, 28 days post last dose of pomalidomide. All analyses detailed in this SAP will be conducted using Statistical Analysis Systems® (SAS®) version 9.2 or higher, except for the PK analysis which will be conducted using PK software (Phoenix WinNonlin 6.4 or higher, and other software as appropriate).

3. STUDY OBJECTIVES

3.1. Primary Objective

The primary objective of the study is:

- To identify potential tumor type(s) for further development by establishing the preliminary efficacy of pomalidomide in children and young adults with recurrent or progressive primary brain tumors within four distinct tumor types.

3.2. Secondary Objectives

The secondary objectives of the study are:

- To evaluate the safety (type and rate of treatment-related toxicity) of pomalidomide within the study populations;
- To estimate the long-term efficacy of pomalidomide treatment.

3.3. Exploratory Objective

The exploratory objective of the study is:

- To assess the PK of pomalidomide in children and young adults with recurrent or progressive primary brain tumors.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a Phase 2 multicenter, open-label, study to assess efficacy, safety and PK of pomalidomide in children and young adults aged 1 to 20 years, inclusive, with one of four types of recurrent or progressive primary brain tumors. Pomalidomide will be administered as gelatin capsules and oral suspension to subjects once daily on days 1 to 21 of a 28-day cycle.

The study will consist of four tumor types, one for each of the following primary brain tumors: high-grade glioma, medulloblastoma, ependymoma, and DIPG. Enrollment and treatment of subjects in each of these four tumor types will run in parallel to one another.

The primary endpoint is the objective response and long-term stable disease rate (ORSDR), defined as the proportion of subjects achieving either an objective response (OR), either a partial response (PR) and/or a complete response (CR), or a long-term SD, defined as SD maintained for ≥ 6 cycles of pomalidomide (≥ 3 cycles for the DIPG tumor type/disease indication).

Each tumor type/disease indication incorporates the Simon's Optimal Two-stage study design.

During the study, a data monitoring committee (DMC) will convene on a regular basis to review safety data and to make recommendations about the study continuation or certain tumor type/disease indication as appropriate, based on the totality of the safety data and interim analysis decision-making data (if needed).

The study will be conducted in compliance with the International Council for Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use/Good Clinical Practice (GCP) and applicable regulatory requirements.

The study will consist of 3 periods: Screening Period, Treatment Period, and Follow-up Period, outlined below (Figure 1):

Screening Period

The Screening Period will start from the time of signing the informed consent form (ICF)/informed assent form (IAF) and will last no more than 28 days, at which time the Treatment Period will begin (Cycle 1 Day 1). The subject's screening procedures are to occur during the Screening Period within 28 days prior to dosing on Cycle 1 Day 1.

Treatment Period

Subjects meeting all eligibility criteria will then enter the Treatment Period and start pomalidomide treatment. Subjects must start treatment within 28 days of signing the ICF/IAF. For all subsequent visits, an administrative window of ± 3 days is permitted, unless otherwise noted for a particular assessment.

Pomalidomide will be administered as monotherapy, gelatin capsule or oral suspension, once daily on Days 1 to 21 of a 28-day cycle. The treatment will be given for up to 24 cycles, or until disease progression (PD), the subject begins a new anticancer treatment, withdrawal of parent/guardian/subject consent/assent, parent/guardian/subject refusal, physician decision,

toxicity that cannot be managed by dose delay or dose reduction alone, or the study ends for any reason.

Follow-up Period

Following treatment discontinuation, all subjects will be followed for 28 days from last pomalidomide dose date for safety and monitoring of adverse events (AEs). This data will be collected at the 28-Day Post Treatment Safety Follow-up visit.

Follow-up will continue for up to 5 years from the data of last subject enrollment into the study regardless of tumor type/disease indication, for disease and survival status, start of any new anticancer therapies, serious adverse events (SAEs) and second primary malignancies (SPM). Subjects will be followed every 3 months during the Follow-up Period.

4.2. Study Endpoints

The endpoints of the study are listed below:

- Primary endpoint
  - Objective response and long-term stable disease rate
- Secondary endpoints
  - Objective response rate
  - Long-term stable disease rate
  - Duration of response
  - Progression-free survival
  - Overall survival
  - Safety
- Exploratory endpoints
  - Pomalidomide PK characterization

4.3. Stratification, Randomization and Blinding

This is an open-label, single therapy study. Treatment assignment does not require randomization, blinding, or stratification.

4.4. Overall Study Design and Plan

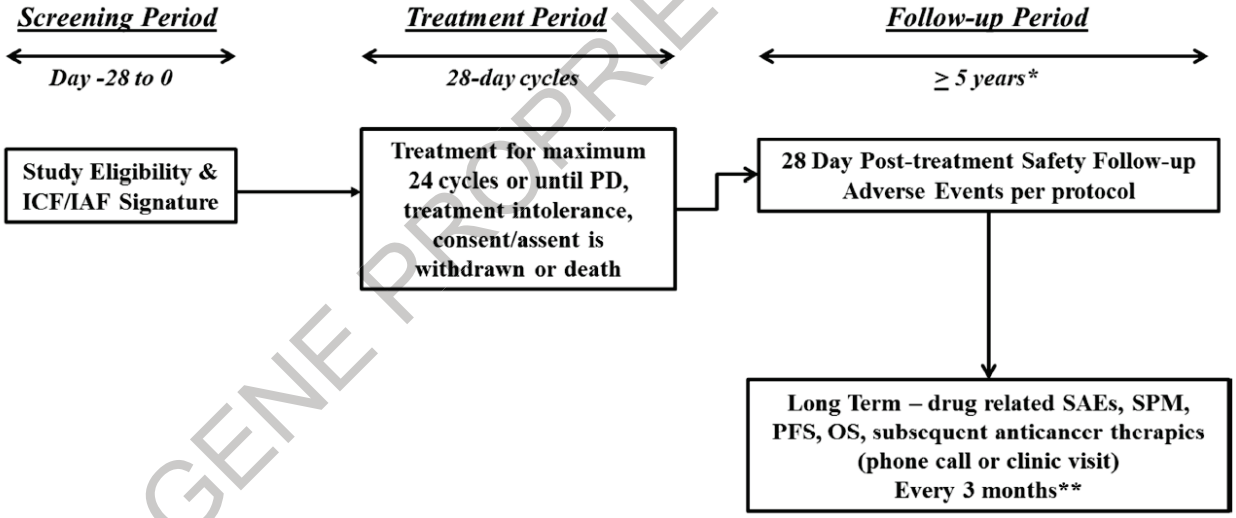
Each tumor type/disease indication incorporates the Simon's Optimal Two-stage study design incorporating the following parameters: significance level of 5%, 90% power and a lower and upper boundary of interest of 10% and 40%, respectively, of the primary endpoint. Based on these boundaries, each tumor type/disease indication will enroll up to 20 subjects eligible for the primary endpoint; 9 in stage one and 11 in stage two. Subjects not eligible for the primary endpoint, ie, not contained within the Response Population, If the number of subjects observed with either an OR or long-term SD according to central response review is ≥ 2, then enrollment shall continue into stage two; otherwise enrollment will close to that specific tumor type/disease

indication. At the end of stage two, if ≥ 5 out of 20, ie, the target ORSDR ≥ 25%, of the subjects enrolled across stage one and stage two combined are observed as having an OR or long-term SD then the treatment will be declared positive in that given tumor type/disease indication; otherwise the treatment will be considered negative in that given tumor type/disease indication (

Figure 2).

If, in a given tumor type/disease indication, by the time the eighteenth subject becomes evaluable for the primary endpoint and only two subjects have been observed across stage 1 and stage 2 combined as having either a OR or long-term SD then enrollment to that tumor type/disease indication will be stopped due to a lack of efficacy.

Figure 1: Overall Study Design

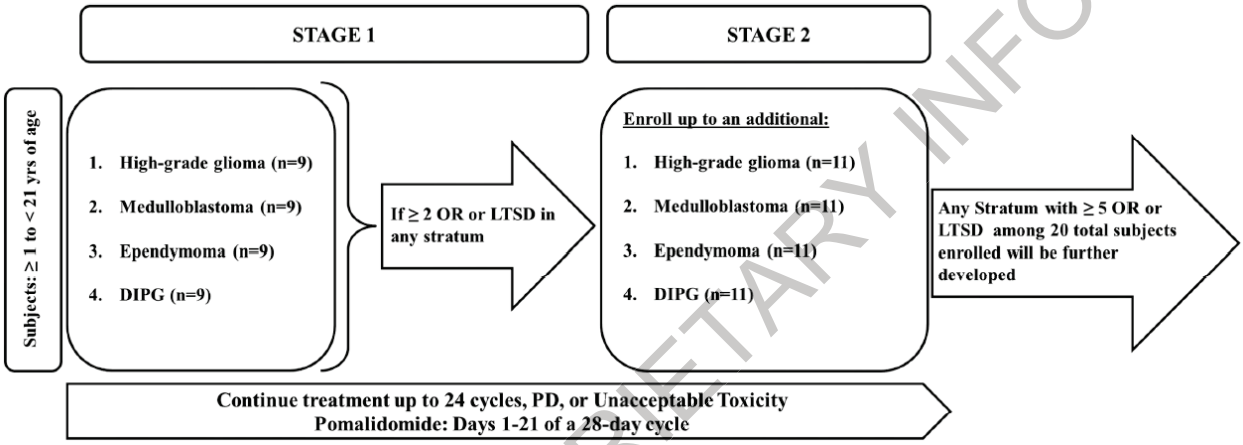


ICF=informed consent form, IAF=informed assent form, MRI=magnetic resonance imaging, OS=overall survival, PD=disease progression, PFS=progression-free survival, SAE=serious adverse event, SPM=second primary malignancy.

*From last subject enrolled

**Subjects without a PD at time of treatment discontinuation will continue to be followed for MRI tumor assessment (every 6 months for the first year from treatment discontinuation, then annually thereafter).

Figure 2: Simon's Optimal Two-stage Parallel Phase 2 Study Design



DIPG=diffuse intrinsic pontine glioma, OR=objective response, PD=progressive disease, LTSD= Long-term stable disease.

5. DEFINITION OF ANALYSIS POPULATIONS

- Informed Consent/Assent Population

The Informed Consent/Assent Population will consist of all subjects with signed informed consent/assent provided. The Informed Consent/Assent Population will be used for describing the disposition of subjects with signed informed consent/assent.

- Response Population

The Response Population will consist of all subjects enrolled who meet eligibility criteria relevant to efficacy, and that received at least one cycle of pomalidomide if not discontinuing therapy earlier due to a PD. The Response Population will be used for analysis of the primary endpoint.
Subjects not eligible for the Response Population due to study ineligibility will be identified by the Celgene clinical team and the subject identification number and reason for exclusion will be logged in an excel sheet for incorporation in study outputs.

- Intent-to-treat Population

The Intent-to-treat (ITT) Population will consist of all subjects enrolled regardless of whether the subject received the assigned study treatment or not. The ITT Population will be used for analysis of efficacy endpoints. The ITT Population will only be invoked if there is at least one subject that enrolled into the study but did not receive pomalidomide, in which case analysis of efficacy endpoints will be based on the Safety Population.

- Safety Population

The Safety Population will consist of all subjects that received at least one dose of pomalidomide. The Safety Population will be applied to the analysis of all safety and efficacy endpoints.

- Pharmacokinetic Population

The PK Population will include all subjects who received at least one dose of pomalidomide and have at least one measurable pomalidomide plasma concentration. The evaluable subjects in the PK Population will be included in the PK data analysis.

6. STATISTICAL METHODOLOGY FOR EFFICACY

Tables will be provided to describe the efficacy endpoints for the Response Population, Safety Population and ITT Population; the ITT Population will only be invoked if at least one of the subjects enrolled does not receive a single dose of pomalidomide. In addition, analysis of the primary endpoint, ORSDR, will be based primarily on the Response Population and decision making such as go/no-go into stage 2 will be based on the analysis using this analysis population. Tables will present data by tumor type/disease indication separately and not in aggregate. Listings will display response assessment data for the ITT Population.

Efficacy endpoints reliant on disease assessments will be based on the independent central response assessments.

In instances where disease assessments are reliant on measurements being collected over a series of days, the last day a measurement is recorded will be used as the date for documentation of the CR, PR, SD or PD.

Missing efficacy data will not be imputed.

6.1. Analysis of Primary Efficacy Endpoint

6.1.1. Objective Response and Long-term Stable Disease Rate

The ORSDR is defined as the percentage of subjects that achieve either a CR, PR or SD maintained for ≥ 6 cycles (≥ 3 cycles for the DIPG tumor type/disease indication) as their best response, divided by the total number of subjects available for the analysis within the given population, eg, subjects contained within the Response Population (primary analysis), the ITT Population, and the Safety Population as outlined within Section 5 of this SAP. The ITT Population will not be used should all enrolled subjects have received at least one dose of study drug. Non-responder subjects are considered subjects with a PD as best response, subjects not having a postbaseline assessment or subjects having not evaluable recorded on their postbaseline assessment(s). The corresponding 2-sided, 95% Clopper-Pearson confidence interval (CI) will also be provided.

Calculation of SD duration starts at the time of first dose of pomalidomide and continues until the date of the first observation of PD is recorded or death due to any cause, regardless of whether the subject achieves a CR and/or PR within that period, or until the date of the last disease assessment if no PD or death is recorded; if the difference is ≥ 6 cycles (≥ 3 cycles for the DIPG tumor type/disease indication), ie, the subject has not had a documented PD before Cycle 7, Day 1 (Cycle 4, Day 1 for the DIPG tumor type/disease indication) and has completed 6 cycles of pomalidomide (3 cycles for the DIPG tumor type/disease indication), then the SD will be considered as being maintained for ≥ 6 cycles (≥ 3 cycles for the DIPG tumor type/disease indication).

For identification of PD for this SD duration calculation, PD is classified as a PD as observed during a response assessment (both during the Treatment Period and the Follow-up Period if applicable); the first time this occurrence is observed is selected as the PD date.

Disease assessments recorded on or after start of a new anticancer therapy will not be considered, nor will disease assessments reported after a PD has been observed.

6.2. Analyses of Secondary Efficacy Endpoints

6.2.1. Objective Response Rate

Objective response rate (ORR) is defined as the percentage of subjects that achieve a CR or PR as their best response, divided by the total number of subjects available for the analysis within the given population, eg, subjects contained within the ITT Population which is formed of all subjects enrolled into the study, the Safety Population which is formed of all subjects receiving at least 1 dose of pomalidomide as outlined within Section 5 of this SAP, and the Response Population which is formed of all subjects completing at least one cycle of study therapy if having not discontinued since the first dose due to either disease progression or relapse and having satisfied the study inclusion and exclusion criteria. The corresponding 2-sided, 95% Clopper-Pearson CI will also be provided.

Disease assessments recorded on or after start of a new anticancer therapy will not be considered, nor will disease assessments reported after a PD has been observed.

In addition, best overall response will be summarized by number and percentage of a subject's best response that meets one of the following categories: (ordered from best response to worst response) CR, PR, SD, PD, or not evaluable. The number of subjects achieving a SD as their best response will also be sub-categorized by the number of subjects with a SD maintained for at ≥ 6 cycles (≥ 3 cycles for the DIPG tumor type/disease indication).

6.2.2. Long-term Stable Disease Rate

Long-term SD rate is defined as the percentage of subjects that achieve a SD maintained for ≥ 6 cycles (≥ 3 cycles for the DIPG tumor type/disease indication), divided by the total number of subjects available for the analysis within the given population, eg, subjects contained within the ITT Population which is formed of all subjects enrolled into the study, the Safety Population which is formed of all subjects receiving at least 1 dose of pomalidomide as outlined within Section 5 of this SAP, and the Response Population which is formed of all subjects completing at least one cycle of study therapy if having not discontinued since the first dose due to either disease progression or relapse and having satisfied the study inclusion and exclusion criteria. The corresponding 2-sided, 95% Clopper-Pearson CI will also be provided.

Calculation of stable disease duration starts at the time of first dose of pomalidomide and continues until the date of the first observation of PD is recorded or death due to any cause, regardless of whether the subject achieves a CR and/or PR within that period, or until the date of the last disease assessment if no PD or death is recorded; if the difference is ≥ 6 cycles (≥ 3 cycles for the DIPG tumor type/disease indication), ie, the subject has not had a documented PD before Cycle 7, Day 1 (Cycle 4, Day 1 for the DIPG tumor type/disease indication) and has completed 6 cycles of pomalidomide (3 cycles for the DIPG tumor type/disease indication), then the SD will be considered as being maintained for ≥ 6 cycles (≥ 3 cycles for the DIPG tumor type/disease indication).

For identification of PD for this endpoint, PD is classified as a PD as observed during a response assessment (both during the Treatment Period and the Follow-up Period if applicable); the first time this occurrence is observed is selected as the PD date.

Disease assessments recorded on or after start of a new anticancer therapy will not be considered, nor will disease assessments reported after a PD has been observed.

6.2.3. Duration of Response

Duration of response (DoR) will be presented in weeks is defined as the duration from initial response (either a CR or PR) to documented PD or death due to any cause, whichever occurs first. The response criteria should be defined in the protocol prior to the start of the study. Duration of response for subjects last known to be alive without PD is censored at the date of last adequate response assessment, or at the start of a new anticancer therapy, whichever occurs first.

The underlying analysis population is confined to those who have responded.

For identification of PD for this endpoint, PD is classified as either a PD as observed during a response assessments (both during the Treatment Period and the Follow-up Period if applicable), or as a PD as recorded on the treatment discontinuation and/or the study discontinuation eCRF; the first time this occurrence is observed is selected as the PD date.

Duration of response will be summarized by median DoR time, along with the corresponding 95% CI, calculated using Kaplan-Meier methods (the estimate of variance will be calculated using Greenwood's formula) (Kaplan and Meier, 1958) for each tumor type/disease indication separately. The Kaplan-Meier curve for DoR will be presented graphically. The proportion remaining progression/death free at 3, 6, 9, 12, 18, and 24 months will be reported and the corresponding standard error provided.

Due to the low anticipated number of subjects and events/censoring, additional summary statistics will be provided, including the arithmetic mean, median, standard deviation (StdDev), first quartile (Q1), third quartile (Q3), minimum (Min), and maximum (Max) values.

Disease assessments recorded on or after start of a new anticancer therapy will not be considered, nor will disease assessments reported after a PD has been observed.

6.2.4. Progression-free Survival

Progression-free survival (PFS) will be presented in weeks and is defined as the time from the date of first pomalidomide dose until the date a PD is first observed or date of death (any cause), whichever occurs first. Subjects who do not have a PD or have not died at the time of an analysis will be censored at the time of their last disease assessment or at the time of start of new anticancer therapy, whichever occurs first.

For the purpose of identification of a PD for this endpoint, PD is classified as either a PD as observed during a response assessments (both during the Treatment Period and the Follow-up Period if applicable), or as a PD as recorded on the Disposition – Treatment and/or the Disposition – Follow-up eCRF; the first time this occurrence is observed is selected as the PD date.

Progression-free survival will be summarized by median progression-free time along with the corresponding 95% CI, calculated using Kaplan-Meier methods (the estimate of variance will be calculated using Greenwood's formula) (Kaplan and Meier, 1958) for each tumor type/disease indication separately. The Kaplan-Meier curves for PFS will be presented graphically. The number and percentage of total disease progression/deaths, as identified for PFS events will be summarized. The proportion remaining progression/death free at 3, 6, 9, 12, 18, and 24 months will be reported and the corresponding standard error provided.

Due to the low anticipated number of subjects and events/censoring, additional summary statistics will be provided, including the arithmetic mean, median, StdDev, Q1, Q3, Min, and Max values.

6.2.5. Overall Survival

Overall survival (OS) will be presented in months and is defined as the duration in months from the date of first pomalidomide dose to the date of death (any cause). Subjects who are alive at the time of analysis will be censored at the last known time that the subject was alive. Overall survival will be summarized by median survival time along with the corresponding 95% CI, calculated using Kaplan-Meier methods (the estimate of variance will be calculated using Greenwood's formula) (Kaplan and Meier, 1958) for each tumor type/disease indication separately. The Kaplan-Meier curve for survival will be presented graphically. The number and percentage of total deaths will be summarized. The survival rate at 3, 6, 9, 12, 18, and 24 months will be reported and the corresponding standard error provided.

Due to the low anticipated number of subjects and events/censoring, additional summary statistics will be provided, including the arithmetic mean, median, StdDev, Q1, Q3, Min, and Max values.

In addition to presentation of OS analysis data, descriptive statistics (arithmetic mean, median, StdDev, Q1, Q3, Min, and Max values) for follow-up time shall be presented for all subjects regardless of survival status, and for only subjects alive at the time of the analysis. Follow-up is defined as the duration in months from the date of first pomalidomide dose to the date of death (any cause), or last known time the subject was known to be alive if alive at the time of analysis or lost to follow-up. Analyses will be based on the ITT Population and/or Safety Population. The ITT Population will not be used should all enrolled subjects have received at least one dose of study drug.

6.3. Subgroup Analysis

There are no subgroup analyses planned to be conducted.

6.4. Pharmacokinetic Analysis

6.4.1. Handling of Pharmacokinetic Data

Posttreatment concentrations that are below the limit of quantitation (BLQ) will be treated as missing. Concentrations assigned a value of missing will be omitted from the descriptive statistics. A concentration value of zero will be excluded from the computation of the geometric

mean (geometric CV%). Geometric CV(%) is calculated as follows: CV(%)=100× SQRT(exp(V)-1), where V denotes the variance of the log-transformed values.

If any subjects are found to be noncompliant with respect to dosing, have incomplete data, or encounter other circumstances that would affect the evaluation of PK, a decision will be made on a case-by-case basis as to their inclusion in the PK analysis. Data excluded from PK analysis will be included in the data listings, but not in the summaries.

In tables and listings for the derived PK data, there should be four decimal places for numerical values below 1, three decimal places for numeric values below 10 but above 1, and two decimal places for numeric values above 10. However, the listings of raw data should not have more or fewer decimal places than the actual data.

6.4.2. Presentation of Pharmacokinetic Results

Listings of PK blood sample collection times, derived sampling time deviations, drug concentrations, and PK parameters will be provided by subject in the PK population.

Plasma concentrations for pomalidomide will be summarized by nominal time points or collection intervals, including sample size (N), mean, StdDev, CV%, geometric mean, geometric CV%, Min, median, and Max. Mean (±StdDev) and individual plot of pomalidomide plasma concentrations versus time will be presented in both linear scale and semi-logarithmic scale.

6.4.3. Population Pharmacokinetic Analysis

Pomalidomide concentration data from this study may be combined with the concentration data from other pediatric studies and literature data to perform a population PK analysis. The between-subject variability for PK parameters may be estimated. If data allow, main PK parameters (clearance and volume of distribution) may be summarized by age as appropriate (eg, ≥ 1 years to < 6, ≥ 6 to < 12, and ≥ 12 years).

6.5. Interim Analysis

Each tumor type/disease indication incorporates the Simon's Optimal Two-stage study design, using a 5% significance level, 90% power, and a lower and upper boundary of 10% and 40%, respectively, for the primary endpoint. For stage one to be evaluated in a given tumor type/disease indication, there must be 9 subjects eligible for the primary endpoint analysis. Subjects If at least 2 subjects are observed as having as either a CR, PR or long-term SD according to central response review, ie, at least 2/9 (≥ 22%), then enrollment in to stage two will continue as planned; otherwise that tumor type/disease indication will be closed to enrollment and the treatment in that tumor type/disease indication considered inefficacious.

If, in a given tumor type/disease indication, none of the first 8 subjects evaluable for the primary endpoint have an OR or long-term SD before the ninth subjects is enrolled, that particular tumor type/disease indication will close to enrollment due to early identification of futility. Similar, if at the time of the interim analysis the required number of subjects observed with an OR or long-term SD is 5 or more, then the enrollment to that given tumor type/disease indication may to stopped due to the required efficacy across stage 1 and stage 2 to declare the study positive in that tumor type/disease indication having been demonstrated early. Each tumor type/disease

indication is run in parallel to each other meaning the interim analysis per tumor type/disease indication may be conducted at different times, as and when the data becomes available for analysis.

7. SUMMARY OF SUBJECT DISPOSITION

The disposition of subjects will be summarized with counts and percentages by tumor type/disease indication and in aggregate. Summaries will include the following:

- Number of Subjects Enrolled, Completed, and Discontinued;
- Number of Subjects in the various analysis population;
- Primary reasons for discontinuation from the treatment, from study, or during follow-up. The reasons for discontinuation should be consistent with the eCRF. This may be done for the ITT Population and Safety populations separately if needed.

A summary table of analysis population will present counts and percentages of the number of subjects by tumor type/disease indication and in aggregate that form the following analysis populations:

- Informed Consent/Assent Population;
- Intent-to-treat Population;
- Response Population;
- Safety Population;
- Pharmacokinetic Population.

A summary table of subjects enrolled by country, and site number will be provided for the ITT Population.

A summary table showing subjects that did not enroll into the study, and reason for non-enrollment, will be provided by tumor type/disease indication for the Informed Consent/Assent Population.

Reasons for completing / discontinuing the Screening Period will be collected on the Disposition – Screening eCRF and will be summarized by tumor type/disease indication and in aggregate for the Informed Consent/Assent Population with the following categories:

- Completed;
- Screen failure;
- Death;
- Adverse event;
- Pregnancy;
- Withdrawal by subject;
- Withdrawal by parent/guardian;

- Lost to follow-up;
- Study terminated by sponsor;
- Protocol violation;
- Physician decision;
- Other.

Reasons for completing / discontinuing the study Treatment Period will be collected on the Disposition – Treatment eCRF and will be summarized by tumor type/disease indication and in aggregate for the ITT Population, the Response Population and the Safety Population with the following categories:

- Completed;
- Death;
- Adverse event;
- Pregnancy;
- Progressive disease;
- Lack of efficacy;
- Recovery;
- Withdrawal by subject;
- Withdrawal by parent/guardian;
- Non-compliance with study drug;
- Lost to follow-up;
- Study terminated by sponsor;
- Protocol violation;
- Physician decision;
- Disease relapse;
- Transition to commercially available treatment;
- Other;
- Site terminated by sponsor.

Reasons for discontinuing the study Follow-up Period / study will be collected on the Disposition – Follow-up eCRF and will be summarized for the ITT Population, the Response Population and the Safety Population with the following categories:

- Completed;

- Death;
- Adverse event;
- Pregnancy;
- Progressive disease;
- Withdrawal by subject;
- Withdrawal by parent/guardian;
- Lost to follow-up;
- Study terminated by sponsor;
- Protocol violation;
- Physician decision;
- Disease Relapse;
- Transition to commercially available treatment;
- Other.

Listings will be provided showing all subjects with signed informed consent/assent showing their status for each study period.

8. DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Demographics and baseline characteristics will be summarized by the ITT Population and the Safety Population per tumor type/disease indication and in aggregate, while medical and treatment histories will be summarized by tumor type/disease indication and in aggregate for the Safety Population; only the Safety Population will be used if all enrolled subjects receive at least one dose of study drug. Baseline clinical characteristics are defined as the latest data collected on or before Cycle 1 Day 1, but before start of treatment. Individual subject listings will be provided to support the summary tables.

8.1. Demographics

Age (years), height, and weight at baseline will be summarized using descriptive statistics (n, mean, median, StdDev, Q1, Q3, Min, and Max). Age category (≥ 1 years to < 6 years, ≥ 6 years to < 12 years, ≥ 12 years), gender, race, ethnicity, and other categorical variables will be summarized by frequency tabulations.

Age will be calculated as follows: age (year) = [(Date of informed consent/assent – Date of Birth + 1) / 365.25]. In the table, age will be presented as an integer. In the listing, age < 2 years will be displayed in month(s), which will be calculated as age (month) = Integer ≤ [(Date of informed consent/assent – Date of Birth + 1) / 30.4375]. Years reached are to be used for categorization.

Use of corticosteroid use at baseline, taken from the Concomitant Medications of Special Interest CRF form, will be indicated in the summary table as well as its use as either physiologic dosing or therapeutic dosing will be presented. Physiologic dosing is defined as no more than 0.75 mg/m^2/day of dexamethasone or equivalent.

Within listings, age will be displayed in years and months as computed following directions given in Appendix 1A, Section 48, while within tables summary statistics for age in years will be used.

Body surface area (BSA) will not be recalculated for tables, listings, and graphs (TLG) presentation but presented based on BSA as calculated and reported by the site per their institutional practice.

8.2. Baseline Disease Characteristics

Baseline disease characteristics will be summarized. Continuous variables will be summarized using descriptive statistics (n, mean, median, StdDev, Q1, Q3, Min, and Max). Categorical variables will be summarized with counts and percentages.

The number and percentage of subjects in each of the following categories will be presented:

- Lansky/Karnofsky performance status at baseline (the 2 performance assessments will be presented separately);
- Tumor type.

8.3. Medical History

A summary of medical history will be presented by Medical Dictionary for Regulatory Activities (MedDRA) version 21.0 or higher system organ class (SOC) and preferred term (PT) for the Safety Population.

Medical and surgical history will be sorted in descending frequency of the SOC based on the aggregate column, and by PT within each SOC; if counts tie, then further by alphabetical order.

8.4. Prior Concomitant and Subsequent Medications/Procedures

Medications initiated prior to the start of study treatment and continued after the start of study treatment will be counted as both prior and concomitant medications.

Tables and listings described in this section will use either the ITT Population or the Safety Population.

8.4.1. Prior Medications and Procedures

Prior medications, therapies and procedures, such as surgeries and transplants, are defined as medications or procedures that were started before the start of the study treatment and either ended before the start of the study treatment or continued after study treatment start. A summary showing the number and percentage of subjects who took prior medications will be presented for the Safety Population by tumor type/disease indication and in aggregate.

Prior medications collected on the "Prior and Concomitant Medication" eCRF page, prior procedures collected on the "Prior and Concomitant Procedures" eCRF page, and prior and concomitant anticancer therapies collected on the "Anticancer Therapies for Brain Tumor – Systemic (Prior)", "Anticancer Therapies for Brain Tumor – Hormonal (Prior)", "Anticancer Procedures for Brain Tumor - Prior Radiation Therapies", "Anticancer Procedures for Brain Tumor - Prior Cancer Surgeries", and "Anticancer Procedures for Brain Tumor - Prior Stem Cell Transplant" eCRF pages will be summarized.

The number of prior therapies and procedures, such as surgeries, will be summarized for prior radiation therapies, prior cancer surgeries, prior systemic anticancer therapies, prior stem cell transplants and other prior anticancer therapies by frequency tabulations based on the Safety Population. Descriptive statistics may be provided also, if needed. The therapies/surgeries with the same sequence/regimen number are counted as 1 prior therapy/surgery.

Prior anticancer therapies / medications will be summarized, if applicable, based on the therapeutic drug class [Anatomical Therapeutic Chemical (ATC) level 1] and preferred name, both based on WHODD March 2018 or later, sorted by frequency of ATC level 1 term and by preferred name within ATC level 1 terms, in the aggregate column; if counts tie, then further by alphabetical order. A table summarizing number of prior therapies and types of therapies will also be provided.

Prior procedures will be summarized, if applicable, based on the MedDRA, version 21.0 or higher, SOC and PT sorted by frequency of SOC and PT within SOC, in the aggregate column; if counts tie, then further by alphabetical order.

Individual listings of prior medications and procedures will be provided to support the tables.

8.4.2. Concomitant Medications and Procedures

Concomitant medications and procedures are defined as medications and procedures, such as surgeries, that were either initiated before the first dose of study drug and continued during the study treatment, or initiated on/after the date of the first dose of study drug and on/before 28 days after the end of the study treatment.

Concomitant medications collected on the "Prior and Concomitant Medication" eCRF page and concomitant procedures collected on the "Prior and Concomitant Procedures" eCRF page will be summarized for the Safety Population by tumor type/disease indication and in aggregate.

Concomitant anticancer therapies / medications will be summarized, if applicable, based on the therapeutic drug class ATC level 1 and preferred name, both based on WHODD March 2018 or later, sorted by frequency of ATC level 1 term and by preferred name within ATC level 1 terms, in the aggregate column; if counts tie, then further by alphabetical order. A table summarizing number of concomitant therapies and types of therapies will also be provided.

Concomitant procedures will be summarized, if applicable, based on the MedDRA, version 21.0 or higher, SOC and PT sorted by frequency of SOC and PT within SOC, in the aggregate column; if counts tie, then further by alphabetical order. A table summarizing number of concomitant procedures and types of therapies will also be provided.

Individual listings of concomitant medications and procedures will be provided to support the tables.

8.4.3. Subsequent Medications and Procedures

Subsequent medications, therapies and procedures, such as surgeries and transplants, are defined as medications or procedures that were started after the last dose of study treatment. A summary showing the number and percentage of subjects who took subsequent medications will be presented for the Safety Population by tumor type/disease indication and in aggregate.

Subsequent anticancer therapies collected on the "Anticancer Therapies for Brain Tumor - Systemic", "Anticancer Therapies for Brain Tumor - Hormonal", "Anticancer Procedures for Brain Tumor - Radiation Therapies", "Anticancer Procedures for Brain Tumor - Cancer Surgeries", and "Anticancer Procedures for Brain Tumor - Stem Cell Transplant" eCRF pages will be summarized.

The number of subsequent therapies and procedures, such as surgeries, will be summarized for subsequent radiation therapies, subsequent cancer surgeries, subsequent systemic anticancer therapies, subsequent stem cell transplants and other subsequent anticancer therapies by frequency tabulations based on the Safety Population. Descriptive statistics may be provided also, if needed. The therapies/surgeries with the same sequence/regimen number are counted as 1 subsequent therapy/surgery.

Subsequent anticancer therapies / medications will be summarized, if applicable, based on the therapeutic drug class (ATC level 1) and preferred name, both based on WHODD March 2018 or later, sorted by frequency of ATC level 1 term and by preferred name within ATC level 1 terms,

in the aggregate column; if counts tie, then further by alphabetical order. A table summarizing number of prior therapies and types of therapies will also be provided.

Subsequent procedures will be summarized, if applicable, based on the MedDRA, version 21.0 or higher, SOC and PT sorted by frequency of SOC and PT within SOC, in the aggregate column; if counts tie, then further by alphabetical order.

Individual listings of concomitant medications and procedures will be provided to support the tables.

9. STUDY TREATMENTS AND EXTENT OF EXPOSURE

Study treatment and extent of exposure summaries will be provided based on the Safety Population. Descriptive statistics (n, mean, median, StdDev, Q1, Q3, Min, and Max) will be provided for the following pomalidomide exposure parameters: treatment duration, cumulative dose, dose exposure, average daily dose, dose intensity and relative dose intensity. Total number, percentage, and frequency of cycles initiated, total number of doses administered, and dose reduction/interruption will also be presented.

Tables will present data by tumor type/disease indication, and in aggregate, split by cycle and overall across cycles.

Individual subject listings of exposure to study drug will be provided.

9.1. Treatment Duration

The treatment duration (days) is defined as:

[(date of last study drug administration) – (date of first study drug administration) + 1]; if in last cycle and 21 days of dose administered then cycle considered complete and date of last dose adjusted to include an additional 7 days, i.e. date of last dose + 7.

Note, the last cycle relates to the last cycle a given subject received before discontinuing from the study Treatment Period.

9.2. Dose Exposure

Dose exposure (days) is defined as the total number of actual drug administration days.

9.3. Cumulative Dose

The cumulative dose (mg/m^2) is defined as the sum of all doses taken across the Treatment Period.

9.4. Average Daily Dose

Average daily dose will be calculated as:

Cumulative Dose / Dose Exposure.

9.5. Average Dose Intensity

The daily average dose intensity ($mg/m^2/day$) is calculated as:

Cumulative Dose / Treatment Duration.

9.6. Relative Dose Intensity

Relative Dose Intensity is calculated as:

Average Dose Intensity / Planned Dose Intensity.

The pomalidomide planned dose intensity (PDI) is calculated as (2.6 mg/m^2 * 21) / 28.

9.7. Dose Modifications - Reduction/Interruption/Delay/Discontinuation

Dose reductions are identified as an actual scheduled dose as recorded on the study drug record eCRF page, eg, > 0 mg/m^2, while being less than the scheduled dose directly prior to the current administration.

If an interruption happens at the start of a cycle and causes the cycle start to be delayed, it is also called a dose delay. Dose delays will be considered together with dose interruptions. Drug interruption are identified as a non-administered planned dose, eg, planned dose > 0 mg/m^2 while actual dose received = 0 mg/m^2, while being directly followed with an actual administered dose eg, actual dose received > 0 mg/m^2, provided an actual dose had been administered previously, ie, a delay will be identified on Day 1 for Cycle 2 onwards provided Cycle 2 onwards had at least one drug administration. Drug interruptions are identified as the time between Day 1 of a current cycle and the last actual dose date of the preceding cycle being > 8 days.

Dose discontinuations are identified as being where the planned dose is > 0 mg/m^2 while actual dose received = 0 mg/m^2, and no further study dose administered.

The overall number and percentage of subjects who have at least one dose reduction/interruption/discontinuation of pomalidomide will be provided for each reason given. Time to first dose reduction/interruption/discontinuation due to any reason will be descriptively provided. Time to first dose reduction/interruption due to AE will also be descriptively provided (n, mean, median, StdDev, Q1, Q3, Min, and Max).

9.8. Overdose

On a per dose basis, an overdose is defined as the following amount over the protocol-specified dose of pomalidomide assigned to a given subject, regardless of any associated AEs or sequelae.

- 10% over the protocol-specified dose

On a schedule or frequency basis, an overdose is defined as anything more frequent than the protocol-required schedule or frequency.

Complete data about any overdose, regardless of whether the overdose was accidental or intentional, will be collected on the eCRF page “Investigational Drug Overdose” and will be presented in a listing.

10. PROTOCOL DEVIATIONS/VIOLATIONS

Protocol deviation and protocol violation categories will be defined by the Celgene CSR and/or Clinical Research Physician (CRP). CCI will identify and manage protocol deviations and protocol violations in a protocol deviation / protocol violation tracker. Additional deviations and violations may be identified by the Celgene CRS and/or CRP during their review of study outputs such as patient profiles and listings. This adjudicated protocol deviation/violation tracker will be maintained by CCI in an excel file and used for analysis.

Protocol violations will be summarized for the Safety Population using frequency tabulations. Moreover, frequencies will be provided for number of subjects with 1, 2, or > 2 protocol violations.

The summary tables will present data by tumor type/disease indication. A listing of subjects with protocol violations/deviations in the Safety Population will be provided.

11. SAFETY ANALYSIS

The purpose of this section is to define the safety parameters for the study. All summaries of safety data will be conducted using the Safety Population and will be presented by tumor type/disease indication, and in aggregate. Safety measurements will include AEs, clinical laboratory information, vital sign measurements, SPM, pregnancy status, and deaths. Individual subject listings will be provided to support the tables.

11.1. Adverse Events

Adverse Events will be coded according to MedDRA dictionary version 21.0 or higher. The severity of AEs will be graded according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE), version 4.03, May 2009, or later.

All AEs will be recorded by the Investigator from the time the subject signs the ICF/IAF until 28 days after the last dose of pomalidomide and those SAEs made known to the Investigator at any time thereafter that are suspected of being related to pomalidomide.

In the occurrence of partial dates, refer to Appendix A2 Section 4.1 where date the imputation guideline is located.

Treatment-emergent adverse events (TEAEs) are defined as any AE occurring or worsening on or after the first dose of pomalidomide and within 28 days after the last pomalidomide administration date. Adverse events leading to death that occur after 28 days post the last pomalidomide administration but are the end result of an ongoing AE that started during the treatment period, or started prior to first dose of pomalidomide but worsened in severity during the treatment period, are considered treatment-emergent. All TEAEs, AEs leading to IP discontinuation, AEs leading to dose reduction/interruption, AEs related to pomalidomide, and SAEs and AEs leading to death will be summarized by cycle up to a 28-day period after last cycle (refer to Appendix A2 Section 3), as well as by subject worst recorded grade per event type, SOC, PT and grade. A summary of AEs with NCI CTCAE version 4.03 Grade 3 or higher, as well as the most frequent PTs, will also be provided by grade and PT. If a subject experiences the same AE more than once with different severity grade, then the event with the highest grade will be tabulated in "by grade" tables. If a subject experiences multiple AEs under the same PT/SOC, then the subject will be counted only once for that PT/SOC. In addition, AEs with a missing intensity will be presented in the summary table as an intensity category of "Missing". Pretreatment AEs will be summarized by PT and SOC.

11.1.1. Overview of TEAEs

The number and percentage of subjects experiencing TEAEs will be summarized in the following categories, although not limited to,:

- All TEAEs;
- TEAEs with severity of grade 3 and/or 4;
- TEAEs with severity of grade 5 (leading to death);
- TEAEs related to pomalidomide;

- TEAEs related to pomalidomide with severity of grade 3 and/or 4;
- Serious TEAEs;
- Serious TEAEs related to pomalidomide;
- TEAEs leading to pomalidomide dose discontinuation;
- TEAEs leading to pomalidomide dose reduction;
- TEAEs leading to pomalidomide dose interruption.

11.1.2. TEAEs by System Organ Class and Preferred Term

The incidence of TEAEs will be summarized by MedDRA SOC and PT. The intensity of AEs will be graded 1 to 5 according to the NCI CTCAE.

Tables summarizing the incidence of TEAEs will be generated for each of the following, although not limited to,:

- All TEAEs;
- TEAEs by severity;
- TEAEs with severity of grade 3 and/or 4;
- TEAEs with severity of grade 5 (leading to death);
- TEAEs related to pomalidomide;
- TEAEs related to pomalidomide by severity;
- TEAEs related to pomalidomide with severity of grade 3 and/or 4;
- Serious TEAEs;
- Serious TEAEs related to pomalidomide;
- TEAEs leading to pomalidomide dose discontinuation;
- TEAEs leading to pomalidomide dose reduction;
- TEAEs leading to pomalidomide dose interruption;
- TEAEs by cycle onset.

System organ classes are sorted by descending order of frequency of SOC, and by descending order of frequency of PT within SOC, according to the overall column.

Treatment emergent adverse events, treatment-related TEAEs, TEAEs of Grade 3 or 4, and treatment-related TEAEs of Grade 3 or 4 will also be analyzed within the following age subgroups:

- Age category ($\geq$ 1 years to $<$ 6 years, $\geq$ 6 years to $<$ 12 years, and $\geq$ 12 years.

Listing of AE, SAE, SAE of special interest and AE leading to treatment discontinuation will be provided in separated displays, showing the day in relation to the first dose of pomalidomide that the AE began/ended.

11.2. Adverse Events of Special Interest

Selected TEAEs and serious AEs (SAEs) will form AEs of special interest (AESI), including second malignancies and cardiovascular events, as determined by the mechanism of action, known class effects, or TEAEs observed to date will be summarized. Standardized MedDRA queries (SMQs) will be used in the search strategy for some of the selected AEs of special interest related to study drug, intending to aid in case identification. The groupings of selected AEs, described by one phrase or topic term will be determined by clinicians based on SMQ or relevant search terms and provided to statistician, prior to database lock.

Analysis of AEs of special interest will be presented with tabulations for: summary of TEAEs of interest by category, TEAEs of interest, CTCAE grade 3 or 4 TEAEs of interest, TEAEs of interest related to study medication, CTCAE grade 3 or 4 TEAEs of interest related to study medication, serious TEAEs of interest, serious TEAEs of interest related to study medication, serious CTCAE grade 3 or 4 TEAEs of interest, TEAEs of interest leading to study medication discontinuation, TEAEs of interest by CTCAE maximum grade 1 or 2 and 3 or 4 and TEAEs of interest by CTCAE maximum grade. The following AE of interest categories and preferred terms include, but are not limited to:

- neutropenia;
- febrile neutropenia;
- infection;
- thrombocytopenia;
- hemorrhage and bleeding;
- neuropathy;
- DVT (deep vein thrombosis);
- PE (pulmonary embolism);
- SPM (second primary malignancies);
- muscular weakness;
- glucose intolerance;
- mood alteration;
- cataract;
- cardiovascular events/dysrhythmia;
- fluid retention/edema;
- hematopoietic cytopenias.

The following summaries will be provided for above-mentioned TEAEs of special interest:

- All TEAEs;
- TEAEs with severity of grade 3 and/or 4;

- TEAEs related to pomalidomide;
- Serious TEAEs;
- Serious TEAEs with severity of grade 3 and/or 4;
- Serious TEAEs related to pomalidomide.

All AESIs will be identified by appropriate MedDRA PT.

11.3. Deaths

Deaths will be coded according to MedDRA version 21.0 or higher.

Tables summarizing the frequency and percentage of deaths by primary cause of death as reported on the Death eCRF, will be generated by tumor type/disease indication, and in aggregate for each of the following:

- All deaths;
- All death during the Treatment Period (defined as deaths from first pomalidomide dose date to 28 days after the last dose of pomalidomide);
- All death after 28 days after end of treatment.

The incidence of deaths will be subject listings showing MedDRA SOC and PT.

11.4. Second Primary Malignancies

Second primary malignancies are monitored as events of interest and reported as SAEs as an added safety assessment measure. Second primary malignancies are any occurring regardless of relationship to study drug during the conduct of the study including up to 5 years after last subject enrollment date.

Events of SPMs will be tabulated for the following categories:

- All SPMs (invasive and non-invasive);
- All invasive SPMs (hematologic and solid tumor);
- All hematologic SPMs (acute myeloid leukemia, myelodysplastic syndromes, B-cell malignancies, and other hematologic cancers);
- All solid tumor SPMs;
- All non-invasive SPMs (non-melanoma skin cancers).

For each of the above SPM categories, SPMs will be further tabulated using the MedDRA PT. Each subject is counted only once within each SPM category as well as within each PT.

Additionally, the number and percentage of subjects with SPMs who died and those who did not die will be tabulated by SPM category.

It should be noted that these analyses with regard to SPMs are based on the number of subjects with at least one SPM and not the total number of SPMs.

For each SPM category, time to onset will be calculated as time (in months) from the start of the study treatment to the onset of the SPM for each affected subject. For the subjects with more than one new malignancy within an SPM category, the onset of the earliest SPM will be used. Time to onset will be summarized descriptively for each SPM category (n, mean, median, StdDev, Q1, Q3, Min, and Max).

A scatter plot to graphically display the time to onset of hematologic and solid tumor SPMs for each SPM by tumor type/disease indication will be provided.

For each SPM category, the incidence rate per 100 person-years will be calculated as: (the number of subjects with any SPM in the SPM category/total person-years)*100. Total person-years are defined as the total time from the date of first treatment to the first onset date of the specified SPM for subjects with the specified SPM plus the total time from the date of first treatment to the date of the last follow-up or death for subjects without the specified SPM. Incidence rates per 100 person-years and the 95% confidence intervals will be calculated for each tumor type/disease indication and SPM category. Confidence interval at 95% level for the incidence rate per 100 person-years is calculated as follows: incidence rate*exp{+/-1.96*n^(-1/2)}.

Listings for “Second Primary Malignancies” and for “Second Primary Malignancies Procedures for Cancers Not Under Study” will be produced by Celgene.

11.5. Vital Sign Measurements

Vital signs (including sitting blood pressure, heart rate, respiration, and temperature) will be measured at screening, on Day 1 of each cycle, at the Treatment Discontinuation Visit, and at the 28-Day Post Treatment Safety Follow-up visit. At unscheduled visits, vital signs will be measured. Height, weight and BSA will be measured at screening, on Day 1 of each cycle, at the Treatment Discontinuation Visit, and at the 28-Day Post Treatment Safety Follow-up visit.

Baseline is defined as the latest value collected on or before the date when the first dose of study treatment is administered. If multiple values are present for the same date, the mean of these values will be used as the baseline.

Summary statistics (n, mean, median, StdDev, Q1, Q3, Min, and Max) of observed and change from baseline values will be presented.

Change from baseline in vital sign values by visit will be displayed in cross–tabulations. For each vital sign parameter, the change from baseline to lowest reported value and highest reported value will be presented. In Table 2: Normal Range of Vital Sign Measurements normal ranges are reported.

Temperature in Fahrenheit will be converted to Celsius with the following formula:

- Temperature in Celsius = (temperature in Fahrenheit – 32) * 5/9.

Table 2: Normal Range of Vital Sign Measurements

Test	Age Group (years) [a]	Normal Range (Unit)
Diastolic Blood Pressure	< 2	[34,66] (mmHg)
	2 to 5	[34,74] (mmHg)
	6 to 8	[35,80] (mmHg)
	9 to 13	[37,87] (mmHg)
	14 to 16	[40,91] (mmHg)
	≥ 17	[40,89] (mmHg)
Systolic Blood Pressure	< 2	[58,112] (mmHg)
	2 to 5	[60,125] (mmHg)
	6 to 8	[65,131] (mmHg)
	9 to 13	[68,141] (mmHg)
	14 to 16	[76,153] (mmHg)
	≥ 17	[70,139] (mmHg)
Pulse Rate	1 to 2	[95, 178] (bpm)
	3 to 7	[62, 124] (bpm)
	8 to 15	[48, 110] (bpm)
	≥ 16	[60, 100] (bpm)
Temperature	All	[35, 38] (°C)
Respiratory Rate	1 to 3	[24,50] (BPM)
	4 to 6	[22,34] (BPM)
	7 to 12	[18,30] (BPM)
	13 to 21	[12,16] (BPM)

[a] Years reached at the time of the assessment.

Listings will be provided for all vital sign parameters for the ITT population.

11.6. Pregnancies

Listings of subjects with data from the "Childbearing Potential" and "Pregnancy Test" eCRF pages will be provided.

11.7. Karnofsky or Lansky Performance Status Score

Performance status will be measured using either the Karnofsky performance status (Karnofsky, 1949) or Lansky performance status (Lansky 1987) score (Karnofsky performance status score for subjects ≥ 16 years of age or Lansky performance status score for subjects < 16 years of age) at screening, on Day 1 of each cycle, Treatment Discontinuation Visit, and at the 28-Day Post Treatment Safety Follow-up visit, refer to Appendix A2 Section 58. For performance status scores, shift from baseline to worst value and best score during the treatment period will be displayed for the whole treatment period and by cycle in a summary table for the Safety

Population. Summary tables will show the data presented by tumor type/disease indication, and in aggregate.

Performance status scores will also be presented in a listing for the ITT Population.

12. PRIMARY AND END OF STUDY FINAL ANALYSES

All tables, listings and figures detailed in this SAP will be provided for the primary final analysis that will be conducted when all on treatment subjects will have completed their 28-Day Post Treatment Safety Follow-up visit, 28 days post last dose of pomalidomide.

For the end of study final analysis, all outputs will be rerun once all subjects will have discontinued the follow-up period (up to 5 years after the last subject enrollment date).

REFERENCES

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Kaplan E L and Meier P. Nonparametric estimation from incomplete observations. Journal of the American Statistical Association 1958;53(282):457-481.

Karnofsky DA, Burchenal JH. The clinical evaluation of chemotherapeutic agents in cancer. In evaluation of chemotherapeutic agents. Edited by Macleod CM. New York: Columbia University Press 1949:191-205.

Lansky SB, List MA, Lansky LL, et al. The measurement of performance in childhood cancer patients. *Cancer.* 1987;60(7):1651-6.

APPENDIX A1 – REPORTING CONVENTIONS

The summary tables, listings, and any supportive SAS output will include the explanatory "headers" that indicate, at a minimum:

- protocol number;
- database cutoff date, displayed as DDMONYYYY;
- company name (Celgene);
- page number (Page x of x).

The summary tables, listings, and any supportive SAS output will include the explanatory "footers" that indicate, at a minimum:

- program source (ie, SAS program name, including the path, run date);
- data extraction date, displayed as DDMONYYYY;
- data source (ie, list of datasets used for the display);
- run time (ie, when the program was run), displayed as DDMONYYYY:HH:MM.

The purpose of the data extraction date is to link the output to the database, either active or archived, that is write-protected for replication and future reference. The program run date is the output date which will appear on each output page and will indicate the date the output was generated by the analysis program. Individual source listings will display all the relative values supporting corresponding table(s) and figure(s).

In addition, the following reporting conventions will be implemented:

- Data from all study sites will be combined for analysis;
- Confidence intervals (CIs) will be presented as 2-sided 95% CIs unless otherwise specified;
- Summary statistics will consist of the number and percentage of subjects in each category for discrete variables, and the sample size (n), mean, median, standard deviation (StaDev), minimum (Min), and maximum (Max) for continuous variables and displayed as follows:

```
n                          xx
Mean                       xx.x
StdDev                     xx.xx
Median                     xx.x
Q1, Q3                  xx.x, xx.x
Min, Max                  xx, xx
```

- For analyses where the sample size, n, is 1, the StaDev will be displayed as 'NA';
- All mean and median values will be formatted to 1 more decimal place than the measured value. Standard deviation values will be formatted to 2 more decimal places than the measured value;
- P-values will be rounded to 4 decimal places. P-values that round to 0.0000 will be presented as '<0.0001' and p-values that round to 1.000 will be presented as '>0.9999';

- All percentages will be rounded to 1 decimal place. The number and percentage of responses will be presented in the form xx (xx.x), where the percentage is in the parentheses. In the case the numerator is equal to the denominator, the percentage should be presented as (100) instead of (100.0);
- If the numerator is '0' then show '0'. If the denominator is '0', then show 'NA' - apply this logic for descriptive stats;
- All listings will be sorted for presentation in order of tumor type/disease indication, study site, subject number, and date of procedure or event. Subjects who are not enrolled will be listed as a non-enrolled group after enrolled subjects;
- In listings, a day reported in relation to treatment start but which is unknown due to an unknown/partially reported date, will be presented with a hyphen;
- In listings, unknown/missing dates will be reported as 'unknown', while the unknown part of a partial date will be presented as 'UN';
- All tables will be presented by tumor type/disease indication;
- In tables where a parameter/category is displayed over several lines, the statistic will be presented on the top line;
- All analysis and summary tables will have the analysis population sample size for each treatment group in the column heading (ie, number of subjects) where applicable;
- Baseline is defined as the latest value collected on or before the date when the first dose of study treatment is administered. If multiple values are present for the same date, the mean of these values will be used as the baseline, except for laboratory data, where the value with the worst Common Terminology Criteria for Adverse Events (CTCAE) grade will be set as baseline. For subjects who were not treated, the baseline value will be defined as the latest value collected on or prior Day 1 of the Cycle 1 visit, if available;
- The day of first dose of study drug pomalidomide will be defined as Day 1. For subjects who are not treated, the Cycle 1 Day 1 visit will be defined as Day 1;
- For tables and figures displaying results by visit, only scheduled visits will be considered beside clinical laboratory evaluations. Unscheduled visits will appear only in listings and could be considered in some derivations;
- The title of the TLG will be centrally justified with the analysis population used directly beneath the title of the TLG, while the TLG number will be in the line directly above the TLG title. The TLG number will be preceded with the text 'Table:', 'Listing:' or 'Figure:', depending on the nature of the output;
- The TLG number will not include alphabetical values;
- The title of the TLG should not include a refence to a footnote;
- The TLG footnotes should follow the following convention for ordering footnotes:
    - Abbreviations

  - Additional footnotes
  - Anchored footnotes, i.e. [a], [b], etc.
  - A line break
  - Program Path
  - Data Source / Data Extraction Date / RunTime;
- Each individual footnote should start on a new line, and end with a full stop;
- The use of the text 'Note:', is not permitted in a footnote;
- Abbreviations used in the main body of the TLG or footnote which are which are not explained as part of a footnote will be explained in the first line of footnote(s), i.e. the abbreviations footnote;
- Throughout the TLGs, instead of m^2 or m2, m2 must be used;
- Instead of ≤ and ≥, <= and >= must be used with a space preceding and a space succeeding the symbol;
- References linked to footnotes must be anchored using character instead of numeric values, ie, use [a], not [1];
- Footnotes that explain abbreviations or categories will use '=' without a space on either side, and be separated with a comma and not a semicolon;
- When a footnote refers to something in the table, such as Race, there is no need to say "Race: ", in the footnote itself;
- In the main body of the TLG or the TLG footnote(s), if text is used to demonstrate a range, then use 'to', and not '-', with a space on either side of the word 'to'.

APPENDIX A2 – CONVENTIONS RELATED TO DATES

Following are the general conventions for various computations and imputations for references. Users may need to consult with study team for specific study practices or regulatory guidelines.

1. Handling of Dates

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

- **Procedure Dates** are the dates on which given protocol-specified procedure are performed. They include the dates of laboratory testing, physical examinations, tumor scans, etc. They should be present whenever data for a protocol-specified procedure are present and should only be missing when a procedure are marked as NOT DONE in the database. Procedure dates will not be imputed.
- **Log Dates** are dates recorded in eCRF data logs. Specifically, they are the start and end dates for adverse events and concomitant medications/procedures. They should not be missing unless an event or medication is marked as *ongoing* in the database. Otherwise, incomplete log dates will be imputed according to the rules in section 4.1 and section 4.2 of this Appendix. However, in listings, log dates will be shown as recorded without imputation.
- **Milestone Dates** are dates of protocol milestones such as randomization, study drug start date, study drug termination date, study closure date, etc. They should not be missing if the milestone occurs for a subject. They will not be imputed.
- **Outcome Dates** are dates corresponding to study endpoints such as survival, progression, etc. In most cases they are derived either from a milestone (eg, the survival date is derived from the death date), or a procedure date (eg, the progression date is derived from the date of the tumor scan that was used to determine progression). They may be subject to endpoint-specific censoring rules if the outcome did not occur, but are not otherwise subject to imputation.
- **Special Dates** cannot be classified in any of the above categories and they include the date of birth. They may be subject to variable-specific censoring and imputation rules.

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

2. Calculations Using Dates

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

- Study days after the start day of study drug will be calculated as the difference between the date of interest and the first date of dosing of study drug (eg, pomalidomide) plus 1 day. The generalized calculation algorithm for relative day is the following:
    - If TARGET DATE >= DSTART then STUDY DAY = (TARGET DATE – DSTART) + 1;
    - Else use STUDY DAY = TARGET DATE – DSTART.

      Note that Study Day 1 is the first day of treatment of study drug. Negative study days are reflective of observations obtained during the baseline/screening period. Note: Partial dates for the first study drug are not imputed in general. All effort should be made to avoid incomplete study drug start dates. Some analyses may exclude subjects without study drug start date. The SAP may be amended on a case-by-case basis, including guideline and suggestion such as imputing Day 1 by consent date of treated subject.
- Age (expressed in days) is calculated: AGE = CONSENT – DATE of BIRTH + 1. In practice, age will be transformed to years by dividing the difference by 365.25 days, then truncating.
    - Preference is for using calculated age from clinical database. When not available, calculated age from eCRF or IVRS may be used.
    - Partial birth date: impute missing day as 15th of the month; impute missing month as July; set missing age for missing year. Should the imputed age succeed an earlier assessment date collected for that subject, the imputed month will be set to the month preceding the assessment date.
- Intervals that are presented in weeks will be transformed from days to weeks by using (without truncation) the following conversion formula:

  WEEKS = DAYS /7.
- Intervals that are presented in months will be transformed from days to months by using (without truncation) the following conversion formula:

  MONTHS = DAYS /30.4375.

3. Calculations of Cycles

Treatment will commence on Day 1 and planned cycle lengths are 28 days. Day 1 of treatment is defined as the first day of actual study drug administration. Day 1 of a cycle is defined as day 1 of study drug for the given cycle as recorded on the eCRF.

Cycle end dates are defined as the day before Day 1 of the following cycle, or if on the last cycle then the last day is the last treatment administration date plus 28 days, i.e. the treatment end date plus 28 days. The treatment end date, and the end date of the last cycle, will be calculated as follows:

- For subjects who discontinue prior to the clinical cutoff date, treatment end date is the date of treatment discontinuation from the treatment disposition page in the eCRF;
- For subjects who are still on treatment at the time of study closure or clinical cutoff, the last date of planned cycle (27 days after first dose of the last cycle) will be used as the treatment end date.

The cycle number for each date of interest, eg, AE start date, will be calculated based on the cycle window set by their start and end dates.

The following rules will be implemented for cycle calculations for TEAEs:

- TEAEs present on or after Day 1 Cycle i but before Day 1 of the subsequent cycle belong to Cycle i (where i stands for cycle number);
- All TEAEs that occur between Day 1 of the last cycle and 28 days after last dose administration date will be included only in the last cycle.

4. Guideline of Missing Date Imputation

4.1 Impute Missing Adverse Events / Prior or Concomitant Medications

A. Incomplete Start Date:

Missing day and month

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

Missing day only

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

Missing day, month, and year

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

B. Incomplete Stop Date:

If the imputed stop date is before the start date, then the imputed stop date will be equal to the start date.

Missing day and month

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

- If the year of the incomplete stop date is **prior to** the year of the last dosing date but is the same as the year of the first dosing date, then the first dosing date will be assigned to the missing date.
- If the year of the incomplete stop date is **after** the year of the last dosing date, then January 1 will be assigned to the missing fields.

Missing day only

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

4.2 Imputing Missing Prior/Concomitant Procedures

Prior/concomitant procedures are defined as surgeries and transplants such as stem-cell transplants.

Partially missing start/stop dates for prior/concomitant procedures will be imputed in the analysis dataset for prior/concomitant procedures. If the stop date is complete with no missing year, month, or day, and the partially missing start date imputed by the rule below is after the stop date, then the start date will be imputed by the stop date.

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

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

4.3 Imputing Missing Medical History

Partially missing medical history start dates will be imputed in the derived dataset for medical history. The 16th of the month will be used to impute a partially missing start date that has only the day missing, and July 1st will be used to impute a partially missing start date that has both the month and day missing. Should the imputed date equal or exceed the informed consent/assent date, the imputed medical history date will be set to 1 day prior to the informed consent/assent date.

4.4 Imputing Missing Disease Progression Date

If the day of the disease progression is missing, then the first day of the non-missing month will be assigned to the missing day; if the month or year of the missing date is missing, then the date will not be imputed and treated as missing.

4.5 Imputing Missing Dates for Prior Therapies

Prior therapies are defined as prior radiation therapies, prior systemic anticancer therapies, and other prior anticancer therapies. Should the imputed date equal or exceed the informed consent/assent date, the imputed start date will be set to 2 days prior to the informed consent/assent date, while the imputed end date will be set to 1 day prior to the informed consent/assent date.

A. Incomplete Start Date:

If the start day of any prior therapy date is missing, then the first day of the non-missing month will be assigned to the missing day; if month or year of the missing date is missing, then the date will not be imputed and treated as missing.

B. Incomplete End Date:

Incomplete date of end of last therapy will be imputed using the following rule: If missing day, impute 15th day of the month; if missing month, impute missing month as middle month (or the earlier month of two month if two months tie) between therapy start month and month of cycle 1 day 1. Should the imputed date be within 21 days of cycle 1 day 1, then the imputed date will be re-set to the 22nd day before cycle 1 day 1.

4.6 Imputing Missing Dates for Date of Birth

Partial birth date: impute missing day as 15th of the month; impute missing month as July; set missing age for missing year. Should the imputed age succeed an earlier assessment date collected for that subject, the imputed month will be set to the month preceding the assessment date.

APPENDIX A3 – STUDY SPECIFICS

Table 3: Table of Events

Period	Protocol Reference Section	Screening Period	Treatment Period[b]								Follow-up Period[b]	
			Each 28-day Cycle							End of Treatment (± 3 days)	28-Day Post Treatment Safety Follow-up	Long-term Follow-up (± 14 days)
			Cycles 1 - 2 (± 3 days)				Cycles 3 - 12 (± 3 days)[i]		Cycles 13 - 24 (± 3 days)[i]			
Day		**-28 to 0**	**1**	**8**	**15**	**22**	**1**	**15**	**1**			
Study Entry and General Assessments												
Obtain Informed Consent/Assent	13.3	X	-	-	-	-	-	-	-	-	-	-
Interactive Response Technology	7.3	X	X	-	-	-	X	-	X	X	-	
Enrollment	6.1.5	-	X[o]	-	-	-	-	-	-	-	-	-
Demographics	6.1.2	X	-	-	-	-	-	-	-	-	-	-
Inclusion/Exclusion Criteria	4.2, 4.3	X	X[o]	-	-	-	-	-	-	-	-	-
Complete Medical History	6.1.3	X	-	-	-	-	-	-	-	-	-	-
Prior Disease Therapies and History	6.1.4	X	-	-	-	-	-	-	-	-	-	-
Prior/Concomitant Medication and Procedures	8.0	After signing ICF/IAF and until 28-day post-treatment Safety Follow-up Visit										-
Safety Assessments												
Adverse Events	10	After signing ICF/IAF and until 28-day post-treatment Safety Follow-up Visit										-
Assessment of Second Primary Malignancy	6.2.4.10	After signing ICF/IAF and until end of Long-term Follow-up Visit										
Physical Exam (including vital signs)	6.4.2.1	X	X[c]	-	-	-	X	-	X	X	X	-
Pomalidomide Education and Counseling[d]	6.4.2.9	X	X	-	-	-	X	-	X	X	X	-
Height	6.4.2.2	X	X	-	-	-	X	-	X	X	X	-

Period	Protocol Reference Section	Screening Period	Treatment Period[b]								Follow-up Period[b]	
			Each 28-day Cycle									
			Cycles 1 – 2 (± 3 days)				Cycles 3 - 12 (± 3 days)[i]		Cycles 13 - 24 (± 3 days)[i]	End of Treatment (± 3 days)	28-Day Post Treatment Safety Follow-up	Long-term Follow-up (± 14 days)
Day		**Screening[a]**	**-28 to 0**	**1**	**8**	**15**	**22**	**1**	**15**	**1**		
Body Weight	6.4.2.3	X	X	-	-	-	X	-	X	X	X	-
BSA calculation	**Error! Reference source not found.**	X	X	-	-	-	X	-	X	-	-	-
Lansky/Karnofsky Performance Status	**Error! Reference source not found.**	X	X	-	-	-	X	-	X	X	X	-
Hematology[e]	6.4.2.6	X	X[c]	X	X	X	X	X	X	X	X	-
Serum blood chemistry[e]	6.4.2.6	X	X[c]	X	X	X	X	X	X	X	X	-
Hepatitis B serology (if applicable)	6.4.2.6	X	-	-	-	-	-	-	-	-	-	-
Pulse oximetry (O_2 saturation)	6.4.2.7	X	As clinically indicated									-
Serum or Urine β-hCG Testing (FCBP/FCCBP)[f]	6.4.2.9	X[g]	X[g]	X[o]	X[o]	X[o]	X[o]	X	-	X	X	X	-
Neurological assessment	6.4.2.8	X	X	-	-	-	X	-	X	X	X	-
Treatment Administration, Accountability and Compliance												
Pomalidomide Dispensing	7.2	-	X	-	-	-	X	-	X	-	-	-
Pomalidomide Administration	7.2	-	Days 1-21			-	Days 1-21		Days 1-21	-	-	-

Period	Protocol Reference Section	Screening Period	Treatment Period[b]								Follow-up Period[b]	
			Each 28-day Cycle									
		Screening[a]	Cycles 1 – 2 (± 3 days)				Cycles 3 - 12 (± 3 days)[i]		Cycles 13 - 24 (± 3 days)[i]	End of Treatment (± 3 days)	28-Day Post Treatment Safety Follow-up	Long-term Follow-up (± 14 days)
Day		**-28 to 0**	**1**	**8**	**15**	**22**	**1**	**15**	**1**			
Response Assessments (High-grade glioma, Medulloblastoma and Ependymoma)												
Brain MRI with and without gadolinium	6.4.1	X[h]	-	-	-	-	Day 1 of Cycles 3, 5, 7, 10, 13, 16, 19, 22 and after Cycle 24[i]			X[j]	-	X[k]
Spine MRI with gadolinium	6.4.1	X[h]	-	-	-	-	Day 1 of Cycles 3, 5, 7, 10, 13, 16, 19, 22 and after Cycle 24[l, i]			X[j]	-	X[k]
Cerebrospinal fluid cytology	6.4.1	As clinically indicated[m]										
Response Assessments (DIPG)												
Brain MRI with and without gadolinium	6.4.1	X[h]	-	-	-	-	Day 1 of Cycles 4, 7, 10, 13, 16, 19, 22 and after Cycle 24[i]			X[j]	-	X[k]
Spine MRI with gadolinium	6.4.1	X[h]	-	-	-	-	Day 1 of Cycles 4, 7, 10, 13, 16, 19, 22 and after Cycle 24[i, l]			X[j]	-	X[k]
Cerebrospinal fluid cytology	6.4.1	As clinically indicated[m]										
Pharmacokinetics – Optional												
Optional Pharmacokinetic blood sampling	6.5	-	-	X[o]	X[o]	-	-	-	-	-	-	-
Follow-up												
PFS, DoR, OS, drug related SAEs, SPMs, new anticancer therapies	6.3	-	-	-	-	-	-	-	-	-	-	X[n]

β-hcg = beta human chorionic gonadotropin; BSA = body surface area; DoR = duration of response; IAF = informed assent form; ICF = informed consent form; MRI = magnetic resonance imaging; O_2 = oxygen; OS = overall survival; PFS = progression free survival; SAE = serious adverse event; SPM = second primary malignancy.

[a] Clinical evaluations to establish eligibility can be obtained up to 28 days prior to Cycle 1, Day 1 (first dose of study drug) unless noted otherwise. Brain/Spine MRI assessments can be obtained up to 21 days prior to Cycle 1, Day 1. Assessments should be re-evaluated as needed if there is a change in clinical status.

[b] Deviations within the provided study visit windows are allowed unless noted otherwise for a particular assessment.

[c] Safety laboratory (hematology and serum blood chemistry) and physical examinations do not need to be repeated on Cycle 1, Day 1 if performed within 7 days of starting treatment, unless clinically indicated. FCBP/FCCBP must have pregnancy test performed within 24 hours prior to the initial dosing of pomalidomide.

[d] Can also be conducted verbally via phone from the site. Subjects must also be counseled against sharing pomalidomide and donating blood, semen or sperm during therapy until the 28-day post-treatment Safety Follow-up Visit. Pregnancy counseling and potential risks must be conducted on Day 1 of each cycle prior to pomalidomide dispensing or at a minimum of every 28 days during the Treatment Period.

[e] Subjects who experience toxicity should have appropriate laboratory testing at least twice weekly (3 to 4 days apart or more frequently) until the toxicity has resolved.
[f] Testing with a sensitivity of at least 25 mIU/mL will be performed in FCBP/FCCBP subjects; refer to Section 6.4.2.9 of the protocol for details. The subject may not receive pomalidomide until the Investigator has verified that the result of the pregnancy test performed on Day 1 (within 24 hours prior to treatment) of every cycle is negative.
[g] Obtain 10 to 14 days prior to first dose of study drug and again within 24 hours prior to first dose of study drug. **NOTE:** The pregnancy test 10 to 14 days prior to initiation of pomalidomide may be omitted, at the discretion of the investigator, for any FCCBP/FCBP who has high acuity disease requiring immediate treatment with pomalidomide. The pregnancy test within 24 hours prior to the first dose of pomalidomide is required to be performed.
[h] Screening/baseline MRI can be obtained up to 21 days prior to Cycle 1 Day 1.
[i] Brain/Spine MRIs can be performed within 7 days prior to scheduled timepoint.
[j] Response/MRI assessment will be performed at the End of Treatment Visit only if the subject has discontinued for reasons other than PD and has been more than 8 weeks since their most recent scan/response assessment.
[k] Subjects that discontinue treatment prior to disease progression will be followed with MRI tumor assessments every 6 months from treatment discontinuation for the first year off treatment, then annually thereafter until PD, start of a new anticancer therapy, consent/assent is withdrawn, is lost to follow-up, or death.
[l] If no spinal or leptomeningeal disease is present at screening/baseline, subsequent spine MRIs will be obtained on Day 1 of Cycle 7, 13, 19 (or within 7 days prior to dosing), after completion of Cycle 24 (± 3 days) and as clinically indicated at the discretion of the primary treating physician. If there is spinal or leptomeningeal disease present at screening/baseline, spine MRIs will be obtained at the same time points as the brain MRI.
[m] As clinically indicated to follow disease at the discretion of the primary treating physician. It is recommended to follow at the same interval as required MRIs if positive at screening/baseline.
[n] SPMs should be reported regardless of causality. After treatment discontinuation, all subjects will be followed every 3 months from the 28-Day post-treatment Safety Follow-Up Visit for up to 5 years after the last subject enrolled.
[o] Cycle 1 only

1. Performance Status

Table 4: Performance Status

Karnofsky Scale (age ≥ 16 years)		**Lansky Scale (age < 16 years)**	
Able to carry on normal activity and to work; no special care needed.		Able to carry on normal activity; no special care is needed	
100	Normal no complaints; no evidence of disease	100	Fully active
90	Able to carry on normal activity; minor signs or symptoms of disease	90	Minor restriction in physically strenuous play
80	Normal activity with effort; some signs or symptoms of disease	80	Restricted in strenuous play, tires more easily, otherwise active
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.		Mild to moderate restriction	
70	Cares for self; unable to carry on normal activity or to do active work	70	Both greater restrictions of, and less time spent in active play
60	Requires occasional assistance, but is able to care for most of his personal needs	60	Ambulatory up to 50% of the time, limited active play with assistance/supervision
50	Requires considerable assistance and frequent medical care	50	Considerable assistance required for any active play, fully able to engage in quiet play
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.		Moderate to severe restriction	
40	Disabled; requires special care and assistance	40	Able to initiate quiet activities
30	Severely disabled; hospital admission is indicated although death not imminent	30	Needs considerable assistance for quiet activity
20	Very sick; hospital admission necessary; active supportive treatment necessary	20	Limited to very passive activity initiated by others (eg, television)
10	Moribund; fatal processes progressing rapidly	10	Completely disabled, not even passive play
0	Dead	0	Unresponsive

Source: Karnofsky, 1949; Lansky 1987.

2. Blood Collection for Pharmacokinetic Analysis

Sparse whole blood samples for PK analysis will be collected from consenting subjects at the time points specified in Table 5: PK Sampling Schedule During Cycle 1 Day 1. Blood samples MUST be drawn from the arm contra lateral to the arm with the intravenous infusion of concomitant medications (if applicable). For each PK sample, draw approximately 1 mL blood and prepare plasma by centrifugation at 4°C. The dose of pomalidomide (Cycle 1: Day 8 and 15) should be administered to subjects in the morning at the study center after the collection of the pre-dose PK blood samples. To reduce PK variability on PK sampling days, subjects will be asked not to eat for 2 hours prior and 2 hours after pomalidomide administration.

Table 5: PK Sampling Schedule During Cycle 1 Day 1

Collection Time Relative to Pomalidomide Administration	Collection Window	Cycle 1, Day 8	Cycle 1, Day 15
0 hour (pre-dose)	-90 min	x	x
2 hours	± 30 min	x	x