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Imago BioSciences, Inc.
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A Multi-Center, Open Label Study to Assess the Safety, Steady-State Pharmacokinetics and Pharmacodynamics of IMG-7289 in Patients with Myelofibrosis

Statistical Analysis Plan

Version 2.0

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I. Introduction

A. Background

The *BCR-ABL1*-negative myeloproliferative neoplasms (MPNs) are a family of related neoplastic disorders of bone marrow. The three main chronic *BCR-ABL1*-negative MPNs are polycythaemia vera (PV), essential thrombocythaemia (ET) and primary myelofibrosis (PMF). The cardinal clinical features of these disorders are increased red cell mass in PV, increased platelet count in ET, and bone marrow fibrosis in PMF. The MPNs are clonal disorders arising most frequently from acquired (somatic) mutations in a multipotent haematopoietic stem/progenitor cell resulting in abnormalities in red cell, granulocyte and platelet production often in association with marrow fibrosis and extramedullary haematopoiesis and, in some cases evolution to acute myeloid leukaemia (AML).

There are no specific treatments for the MPNs. The JAK1/2 inhibitor ruxolitinib is approved for the treatment of disease-related symptoms and splenomegaly in adult myelofibrosis (including PMF, PPV-MF and PET-MF) patients. It is effective at alleviating constitutional symptoms, normalizing blood counts and reducing spleen size in many patients. Ruxolitinib does not appear to significantly alter the natural history of the disease but mortality in a three year period is reduced 50% in the high-risk patients. Ruxolitinib is effective only during administration; symptoms recur soon after treatment is stopped. Fibrosis in the marrow is largely unaffected by treatment with ruxolitinib; there is no short-term clinical impact on $JAK2^{V617F}$ allele frequencies, but treatment for more than three years may reduce the allele burden (Deininger *et al*., 2015). Other treatments principally manage symptoms.

IMG-7289 is an orally available, irreversible inhibitor of LSD1, active against LSD1 and human AML cells CCI LSD1, also known as KDM1A, is an enzyme that removes mono- and dimethyl groups from histone (H) H3 at critical lysines (K), K4 and K9 (Shi *et al.*, 2004), thereby regulating chromatin structure and gene expression. *LSD1* is an essential gene; loss of LSD1 activity leads to early embryonic lethality (Wang *et al.*, 2009; Foster *et al.*, 2010). The protein is also needed for regulating the balance between self-renewal and proliferation (Wang *et al.*, 2007). . However, over-expression of *LSD1* messenger RNA (mRNA) and excess LSD1 protein have been observed in many tumour types, including poorly-differentiated neuroblastoma, squamous cell carcinoma, Ewing's sarcoma, AML, neuroendocrine carcinomas and epithelial tumours such as breast, prostate, bladder, small cell lung and colon cancers (Metzger *et al.*, 2005; Kahl *et al.*, 2006; Schulte *et al.*, 2009; Lim *et al.*, 2010). In the *BCR-ABL1*-negative myeloproliferative neoplasms (MPNs) family (including polycythaemia vera (PV), essential thrombocythaemia (ET) and primary myelofibrosis (PMF)), LSD1 was over-expressed mainly in megakaryocytes and erythroid precursors and to a lesser degree in early myeloid cells (Niebel *et al*., 2014).

Treatment of various tumour types in culture with LSD1 inhibitors (LSDi) has been reported to inhibit tumour growth, reduce their potential for migration and

invasion, reduce clonogenic potential and eliminate cancer stem cells, induce markers of differentiation appropriate to the cell lineage, and induce apoptosis (Somervaille and Cleary, 2006; Somervaille *et al.*, 2009; Harris *et al.*, 2012; Zhang *et al.*, 2013). The therapeutic goal for the treatment of MF is to inhibit the activity of LSD1 in haematopoietic cells for only a fraction of the 24-hour dosing cycle.

Proof-of-concept studies were performed in well established, pre-clinical mouse models of PMF. CCI [redacted] This effect is not observed in this model when treating with ruxolitinib. CCI [redacted] The anti-cytokine effects of JAK1/2 inhibition by ruxolitinib were more modest compared to what was achieved with LSDi, CCI [redacted]

CCI [redacted] This effect is not observed in this model when treating with ruxolitinib. CCI [redacted]

This study initiated as a Phase 1/2a study assessing the safety of the starting dose, an CCI [redacted] duration of treatment, and the pharmacokinetic and pharmacodynamic effects of IMG-7289 (under original protocol and amendments 2-4), with transition to a Phase 2b study incorporating changes supported by the Phase 1/2a data (under amendments 4-6).

This study consists of two periods: The Initial Treatment Period, followed by the Additional Treatment Period. In the Additional Treatment Period, which is iterative, treatment may continue in those patients deriving clinical benefit and safely tolerating IMG-7289, as determined by the Principal Investigator.

Patients enrolled in the Phase 1/2a portion of study are treated in the ITP daily for CCI [redacted] if qualified, they may continue to the ATP after a brief washout period, and be treated daily for an additional CCI [redacted] Patients enrolled in the Phase 2b portion of study are treated in the ITP daily for CCI [redacted]; if qualified, they may continue directly to the ATP with no washout period, and be treated daily for an additional 169 days.

The protocol, IMG-7289-CTP-102, describes the general approach to analysis of data from the study. The purpose of this Statistical Analysis Plan (SAP) is to outline the statistical principles which will be used to analyze and present the

data, including definition of endpoints, stopping rules, and analysis populations. Table, Figure, and Listing shells will be supplied in an accompanying document.

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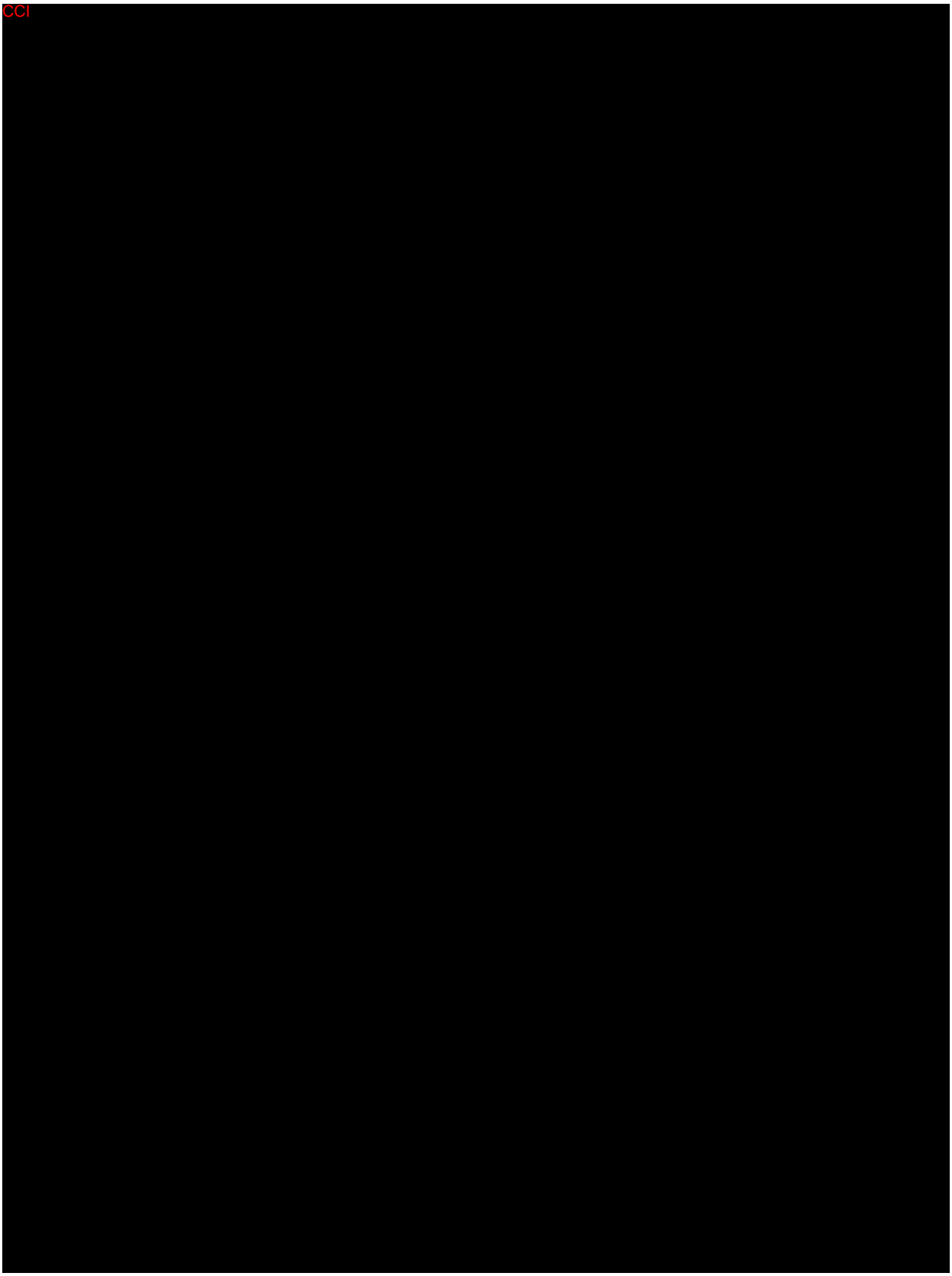

II. Protocol Objectives

The following primary and exploratory objectives will be evaluated in patients with myelofibrosis including primary myelofibrosis (PMF), post-polycythaemia vera-myelofibrosis (PPV-MF), and post-essential thrombocythaemia-myelofibrosis (PET-MF) (collectively referred to as 'MF').

A. Primary

To evaluate in MF patients the effect of IMG-7289 on:

- Safety and tolerability
- Pharmacokinetics (Phase 1/2a only)
- Reduction in spleen volume

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[redacted]

III. Study Endpoints

A. Primary

- The safety and tolerability of IMG-7289 will be assessed by the analysis of adverse events (AEs), as well as changes in physical examinations, vital signs and laboratory values CCI

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  - Changes in physical examinations, vital signs and laboratory values will also be evaluated and assessed from Screening/Baseline until End of Study (EoS)/End of Treatment (ET). Information on the timing of these assessments is presented in the schedule of assessment. CCI

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- Pharmacokinetic (PK) parameters will be determined using serial blood sampling at specified time-points to determine PK effects of IMG-7289 (Phase 1/2a only). Non-compartmental methods of analysis will be used to determine PK parameters following oral dosing of patients. CCI

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- Reduction in spleen volume will be assessed based on spleen volume measured by MRI (or CT scan where applicable) from Day 0, and spleen size measured by palpation from Baseline to each visit where the variables are measured.

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IV. Study Design

A. Design Overview

This is a multi-center, open-label study evaluating the safety, tolerability, steady-state pharmacokinetics and pharmacodynamics of IMG-7289 administered orally once daily in patients with myelofibrosis (MF).

The therapeutic goal for the treatment of MF is to inhibit the activity of LSD1 in haematopoietic cells for only a fraction of the 24-hour dosing cycle sufficient to reduce platelets to a safe level while inhibiting to the greatest extent possible the production, by megakaryocytes, of cytokines and growth factors that drive bone marrow fibrogenesis and symptoms. Considerations for a safe and therapeutic starting dose included chronic toxicology studies, in conjunction with clinical experience of the patients who have received IMG-7289 to date in both IMG-7289-CTP-101 and -102. CCI [redacted]

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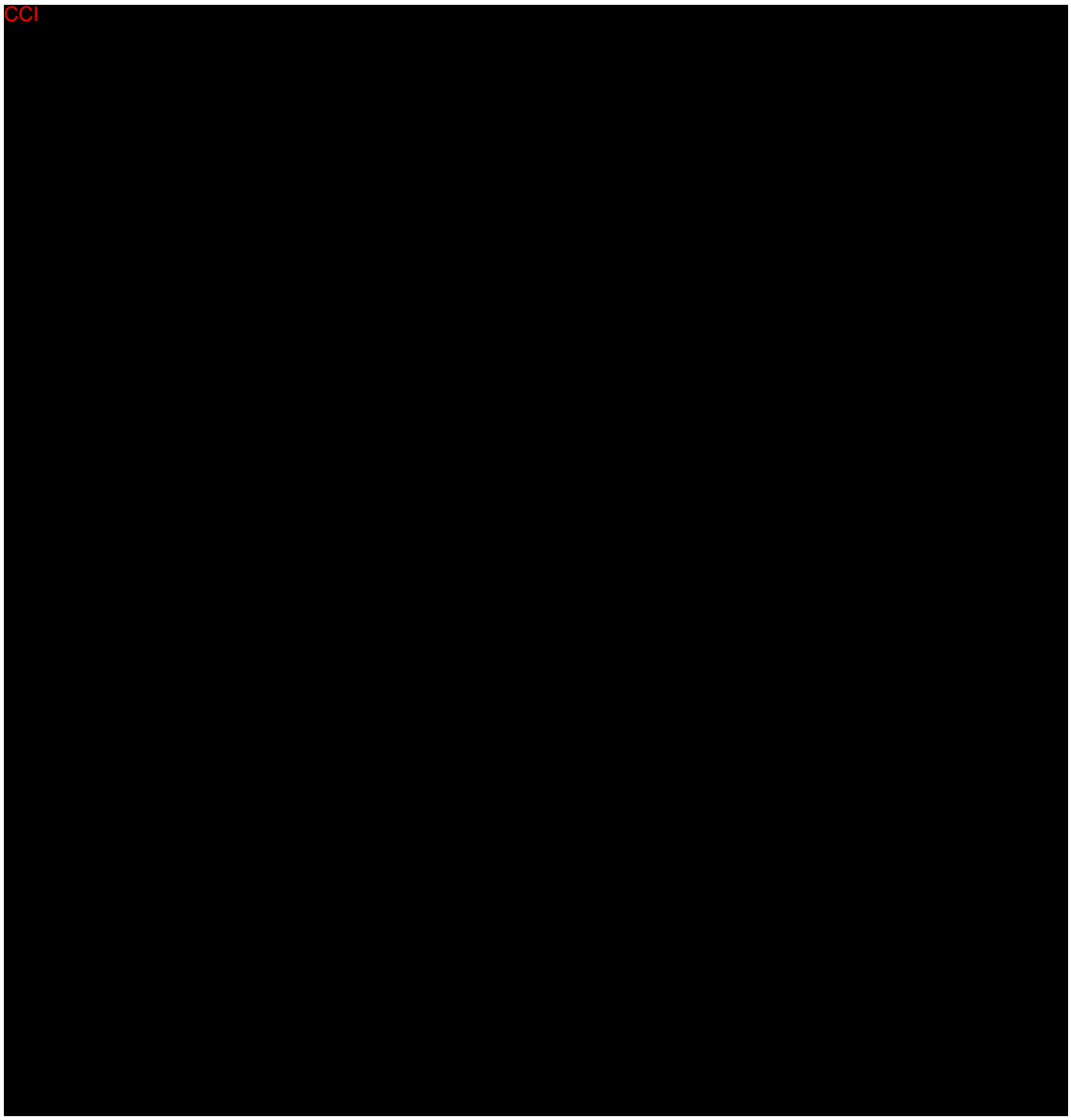

This study initiated as a Phase 1/2a study, assessing the safety of the starting dose, an 85-day duration of treatment, and the pharmacokinetic and pharmacodynamic effects of IMG-7289, with transition to a Phase 2b study including implementation of changes supported by the Phase 1/2a data.

This study consists of two treatment periods: The Initial Treatment Period (ITP), followed by the Additional Treatment Period (ATP); the ATP is iterative, and allows patients to continue treatment if they derive clinical benefit (defined as not meeting progressive disease criteria as per protocol Section **Erreur ! Source du renvoi introuvable.**) and safety tolerating IMG-7289 as determined by the Principal Investigator

Patients enrolled in the Phase 1/2a portion of study are treated in the ITP daily for 85 days; if qualified, they may continue to the ATP after a brief washout period, and be treated daily for an additional 85 days. Patients enrolled in the Phase 2b portion of study are treated in the ITP daily for 169 days; if qualified,

they may continue directly to the ATP with no washout period, and be treated daily for an additional 169 days.

All patients will undergo follow-up period visits, including an End-of-Treatment (EoT) visit on the day of last dose or as soon as possible thereafter, a pre-End-of-Study (EoS) visit approximately 14 days post last dose, and an End-of-Study (EoS) visit approximately 28 days post last dose. Patients that do not enter the Additional Treatment Period, or discontinue early, will undergo follow-up, beginning with an EoT visit.

Patients will be followed closely throughout the study for both Adverse Events (AEs) and signs of toxicity by frequent monitoring of clinical signs and symptoms and by peripheral blood and urine analyses. Pharmacodynamic effects will be closely monitored by frequent haematology assessments of peripheral blood, and requisite bone marrow aspirates and biopsies. Throughout dosing, transfusions may be administered if needed in accordance with standard institutional guidelines.

B. Study Population

The patient population will consist of men and women age 18 or older who have been diagnosed with intermediate-1, intermediate -2 or high-risk primary myelofibrosis (PMF), post-polycythaemia vera myelofibrosis (PPV-MF), or post-essential thrombocythaemia myelofibrosis (PET-MF). Eligible patients who have signed informed consent must have had no prior treatments within a specified period of time and met pre-specified laboratory values for selected parameters, in addition to multiple other required eligibility criteria.

C. Sample Size Predictions

Approximately seventy-five (75) MF patients are expected to be enrolled and treated in the study and a minimum of 45 patients are required to complete the entirety of the Initial Treatment Period (including MRI/CT). This study is designed to make an assessment of the safety, tolerability, and pharmacokinetics of the capsule formulation of IMG-7289. The Phase 1/2a portion of the study was planned for a minimum of 15 patients; with 18 enrolled and treated patients, the Phase 1/2a portion of the study is sufficiently powered to determine mean pharmacokinetic parameters. Given that all pharmacodynamic (PD) metrics are exploratory in nature, the study is not powered to make statements about the statistical significance of any changes observed.

D. Treatment Randomization

This is not a randomized study.

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V. Interventions

A. Clinical Trial Material

The drug product is IMG-7289, a bis-tosylate salt. The free base of IMG-7289 is the active moiety. IMG-7289 will be supplied in capsules of multiple strengths. These strengths, based on IMG-7289 free base, i.e. the active substance, may include: 1 mg, 5 mg, 10 mg, 25 mg, and 50 mg. At Phase 2b, 1 mg capsules are not provided.

B. Study Procedures

Patients will undergo procedures described in protocol Section 9 to assess the study drug safety, pharmacodynamics, and pharmacokinetics in order to achieve the study objectives.

VI. General Analytical Considerations

The statistical analyses will be reported using summary tables, figures, and data listings. Unless otherwise noted, all statistical testing will be two-sided with significance being $p < 0.05$. Continuous variables will be summarized with means, standard deviations, medians, minimums, and maximums. Categorical variables will be summarized by counts and by percentage of patients in corresponding categories. As appropriate and where specified, continuous and categorical variables will be evaluated using the paired t-test, Kruskal-Wallis, Wilcoxon rank sum, Sign rank test, Fisher's exact, or χ^2 tests to assess the significance of differences in haematologic, pharmacodynamics markers, and response. As appropriate and where specified, summary tables will be presented by the type of disease within starting dose, with an "All Patients" summary. Refer to section VI.K for details.

The analyses described in this plan are considered *a priori*, in that they have been defined prior to database lock. If any post-hoc analyses are performed, they will be defined and reported in the CSR.

All analyses will be performed using SAS statistical analysis software version 9.4 or higher of SAS for Windows [SAS Institute Inc; Cary, NC, USA]).

A. Data Sources

All data are collected *via* electronic case report forms (eCRFs) through remote data entry. Section 13.6 of the protocol describes data quality assurance.

B. Definition of Baseline

For analysis purposes, baseline is defined as the last assessment prior to the first dose of study drug. Day 0 is the first day a patient receives study drug. For most measurements, baseline assessments will be taken pre-dose on Initial Treatment Period ITP Day 0. If pre-dose assessments on Day 0 are not available, the most recent prior assessment closest to Day 0 may be substituted in some cases, and unless otherwise specified.

C. Missing Data

For safety and tolerability, missing data, including those not obtained because of death, will be the last value carried forward.

If CTCAE Grade is missing, the event is assumed to be 'Severe' (grade 3). If AE relatedness is missing, the event is assumed to be 'possibly' related.

When relevant, sections below will address how missing data will be handled for the particular analyses. Otherwise, missing data will not be replaced with imputed values.

D. Display and Imputation Methods for Missing Dates

Every effort will be made to query missing dates. However, partial dates are allowed on the eCRF for Adverse Event (AE) onset and resolution dates (only month and year are required), Concomitant Medication (CM) start and stop dates (only year is required), and Prior and Concurrent Cancer Chemotherapy (PCTHX) start and stop dates (only year is required).

Per protocol, Adverse Events (AEs) are captured in the eCRF commencing with the first dose of IMG-7289 through to the End of Study Visit (scheduled for approximately 28 days post last IMG-7289 dose). For records with missing AE onset day, the following procedure will be employed for use in determining whether the AE is treatment-emergent:

- AE onset dates with missing day will be assumed to occur on the first day of the non-missing month, except for AEs occurring in the first month of dosing, in which case the date will be the first day of dosing.

Additionally, if for some reason the start date of an AE is partially or completely missing and the end date of the AE does not indicate that the AE occurred prior to the first dose of IMG-7289, then the determination of treatment-emergent status will be based on the following:

- If the start date is completely missing, then the AE is treatment-emergent.
- If the start year is the same as the year of the first dose of study drug and the start month is the same or after the month of the first dose of study drug, then the AE is treatment-emergent.
- If the start year is after the year of the first dose of study drug, then the AE is treatment emergent.

For records with a missing CM or PCTHX start and/or stop day or month, the following procedure will be employed for use in determining whether the therapy (i.e., medication or chemotherapy) is prior or concomitant/concurrent:

- Therapy start dates with a missing day and non-missing month will be assumed to occur on the *first* day of the non-missing month, except for therapies occurring in the first month of dosing, in which case the date will be the first day of dosing.

- Therapy start dates with a missing day and month will be assumed to occur on the *first* day of the non-missing year (i.e., January 1), except for medications occurring in the first year of dosing, in which case the date will be the first day of dosing.
- Therapies that are not marked as ongoing, and have a stop date with a missing day and non-missing month will be assumed to occur on the *last* day of the non-missing month.
- Therapies that are not marked as ongoing, and have a stop date with a missing day and month will be assumed to occur on the *last* day of the non-missing year (i.e. December 31).

For the listings, AE, CM and PCTHX dates will be listed as collected in the eCRF.

All other data will be reported as they are collected. No imputation methods will be used to replace missing data unless otherwise stated in this document.

Partial transfusion start dates are not permitted, and thus assumptions should not be needed to determine if the transfusion was prior to the first dose of IMG-7289.

E. Multiple Study Centers

There will be no adjustment for multiple study centers in the analysis.

F. Covariate Adjustment in Primary Analysis

There will be no adjustment in the analysis for covariates.

G. Sample Size Reassessment

No sample size reassessment is planned for this study.

H. Interim Analyses and Data Safety Monitoring Committee (DSMC)

No formal interim analysis is planned for this study.

The DSMC reviews safety parameters and pharmacodynamic markers to draw conclusions around the safety and pharmacodynamic effect of IMG-7289. The DSMC responsibilities will remain in effect until study has ended.

The DSMC/SAB also reviews patient dose titrations and may recommend adjustments. At the original starting dose of 0.25 mg/kg/day, two sentinel patients were dosed for 7 days of treatment before initiating enrollment on a rolling basis. Data from the first sentinel patient was reviewed by the DSMC prior to dosing the second sentinel patient. The DSMC/SAB convened within 4 days post-completion of 7 days of treatment for each of the sentinel patients at the original D_s and determined that it was safe for each sentinel patient to continue dosing, and that it was safe for additional patients to begin treatment with IMG-7289.

Additionally, the DSMC convened post-completion of 7 days of treatment of the required three patients at the new starting dose of 0.5 mg/kg/day and determined:

the safety of the new 0.5 mg/kg/day starting dose, and the ITP Day 3 (mid-week) visit could be removed from the visit schedule.

The DSMC is scheduled to meet at least monthly during Phase 1/2a and quarterly during Phase 2b.

I. Multiple Comparisons

No control for the effect of multiple comparisons is planned.

J. Application of Visit Windows

In general, summaries will present the visits that are expected for each dose/cohort. Visits will be represented by treatment period (ITP or ATP) and day within period; for subjects that experience more than one ATP, each ATP will be treated separately (e.g. ATP1, ATP2). If a visit that is presented on a particular page is expected for some dose/cohorts but not others, then the summary will indicate "n/a" for the visits that are not expected for that particular dose/cohort.

If sufficient patients within a phase and cohort have visits that are performed off-schedule, and there is concern that summary by designated visit within period will be misleading due to comparison of assessments that have not had comparable treatment duration within that period, then visit windowing may be utilized for data summarization. In that case, visit windows will be defined by establishing the expected schedule for the dose/cohort, and establishing boundaries for each window as the midpoint between the previous expected visit day and the next expected visit day. Assessments will be slotted for summarization according to the visit windows, rather than the visit designated in the eCRF. If more than one assessment occurs within a particular window, then the assessment closest to the expected visit day will be used. If more than one such assessment exists, then the assessment whose visit designation in EDC is closest to the expected visit designation will be used. If windowing is applied for a given type of assessment, this will be indicated in the footnote of the summary table and the corresponding listing, and the listing will indicate both the visit designation from EDC and the visit window in which the assessment is included.

This methodology may be applied to summaries of laboratory data, vital signs data, and/or symptom scores. As assessment schedules may differ for these assessments, windows may be parameter type-specific.

K. Analysis Populations

Only the Safety population will be considered as analysis population for performing the various analyses. All enrolled patients who received at least one dose of IMG-7289 will be included in the Safety population.

Patients having no post-baseline disease assessment will be defined as NE (not evaluable).

L. Subgroups of Analysis Populations

The summaries and listings will be separated by the starting dose, and type of disease within starting dose. Summaries will include an "All Patients" category for each starting dose, as well as an "All Patients" category for the entire set of patents in the analysis set.

Categories for starting dose are: Phase 1/2a - 0.25 mg/kg/d (amendments 1, 2 and 3); Phase 2b - 0.5 mg/kg/d (amendments 4, 5); and Phase 2b - 0.6 mg/kg/d (amendment 6).

Categories for type of disease are: primary myelofibrosis (PMF), post-polycythaemia vera myelofibrosis (PPV-MF), or post-essential thrombocythaemia myelofibrosis (PET-MF) within starting dose category.

M. Data Display Characteristics

Data displays produced for this study will include two types - summary tables, and data listings. Unless stated otherwise, data listings will be produced for all recorded data. Summary tables will include columns for each starting dose category and each type of myelofibrosis (MF) within the starting dose category, and the ordering of these diseases will be defined in the tables, listings, and figures (TLF) shells document. Summary tables will be produced as specified in the following sections. Additional data listings will be produced for outcome measures that involve extensive procedures to derive the analyzed outcomes.

Data listings will simply list the data that are either recorded on the CRF or derived for each patient. In general, they will be ordered by starting dose category, type of myelofibrosis (MF), patient number, and time of assessment, unless otherwise specified in the display shell. When expedient, additional levels of ordering hierarchy may reflect subsets of assessments within patient. Data listings will not display patient initials.

Summary tables will display summary statistics calculated for each starting dose category and each type of myelofibrosis (MF), and for all patients combined, unless described otherwise in the following sections, or in the display shells. For most summary tables, the types of myelofibrosis (MF) will be presented in separate columns, and the summary statistics of interest will be presented in rows.

Descriptive statistics (sample size, arithmetic mean, standard deviation (SD), median, minimum, maximum) will be calculated for quantitative safety data as well as for the differences from baseline, when appropriate. Counts and percentages will be presented for categorical data.

VII. Patient Accountability

A. Patient Characteristics

Demography. Data collected about the following patient characteristics at the screening/baseline visit will be listed and summarized for the safety population:

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Disease History. Baseline history will be summarized and listed.

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Medical History. Medical Histories will be listed.

Prior Disease Treatment. Data from prior disease treatments will be summarized and listed:

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B. Disposition

Disposition. Patient disposition data will be summarized for the Safety Population by the type of myelofibrosis (MF). Summaries will include:

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C. Protocol Deviations

Protocol deviations and waivers will be provided in a listing.

VIII. Efficacy Analyses

A. Primary Analysis

1. Spleen Volume

Spleen volume (mL) will be measured by MRI (or CT scan where applicable) from Day 0. Descriptive statistics will be presented for actual spleen volume, change from baseline, and percentage change from baseline by visit; and for maximum percentage change from baseline, minimum percentage change from baseline, and best percentage change from baseline will be presented. The best percentage change from baseline is defined as the maximum percentage decrease or the minimum percentage increase if there is no decrease in a patient during treatment.

In addition, an analysis of mean spleen volume will be performed. The mean and its 95% confidence interval (CI) will be presented for the spleen volume (mL), change from baseline, and percentage change from baseline at each visit; and for the best percentage change from baseline. P-value for test to assess change from baseline at each visit will be calculated using paired t-test. P-value for test to assess percentage change from baseline at each visit and the best percentage change from baseline will be calculated using one sample t-test with the hypothesis that the percentage change is 0.

2. Spleen Size

Spleen size (cm) will be measured by palpation at each visit. Descriptive statistics will be presented for actual spleen size, change from baseline, and percentage change from baseline by visit; and for maximum percentage change from baseline, minimum percentage change from baseline, and best percentage change from baseline will be presented. The best percentage change from baseline is defined as the maximum percentage decrease or the minimum percentage increase if there is no decrease in a patient during treatment.

In addition, an analysis of mean spleen size will be performed. The mean and its 95% confidence interval (CI) will be presented for the spleen size (cm), change from baseline, and percentage change from baseline at each visit; and for the best percentage change from baseline. P-value for test to assess change from baseline at each visit will be calculated using paired t-test. P-value for test to assess percentage change from baseline at each visit and the best percentage change from baseline will be calculated using one sample t-test with the hypothesis that the percentage change is 0.

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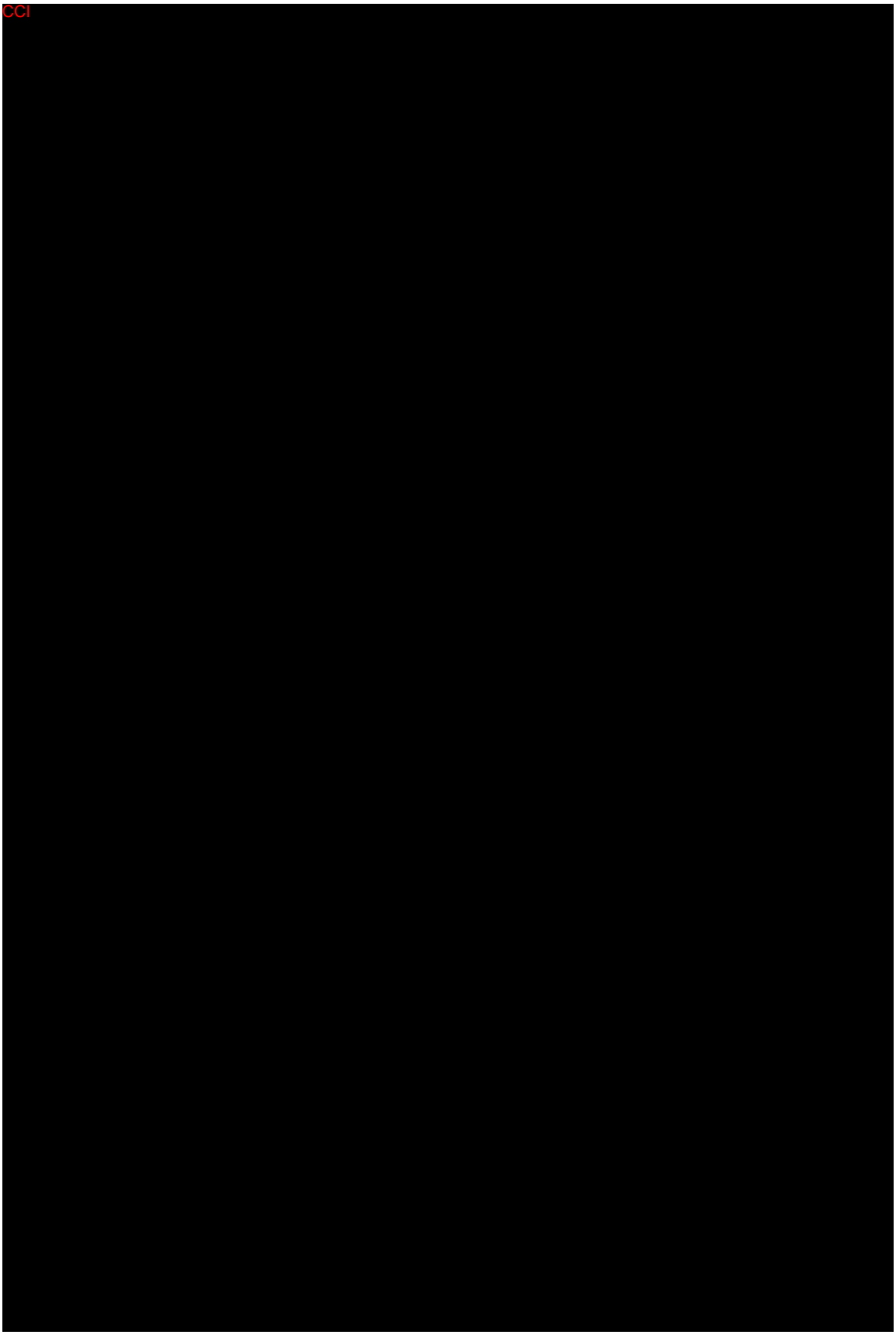


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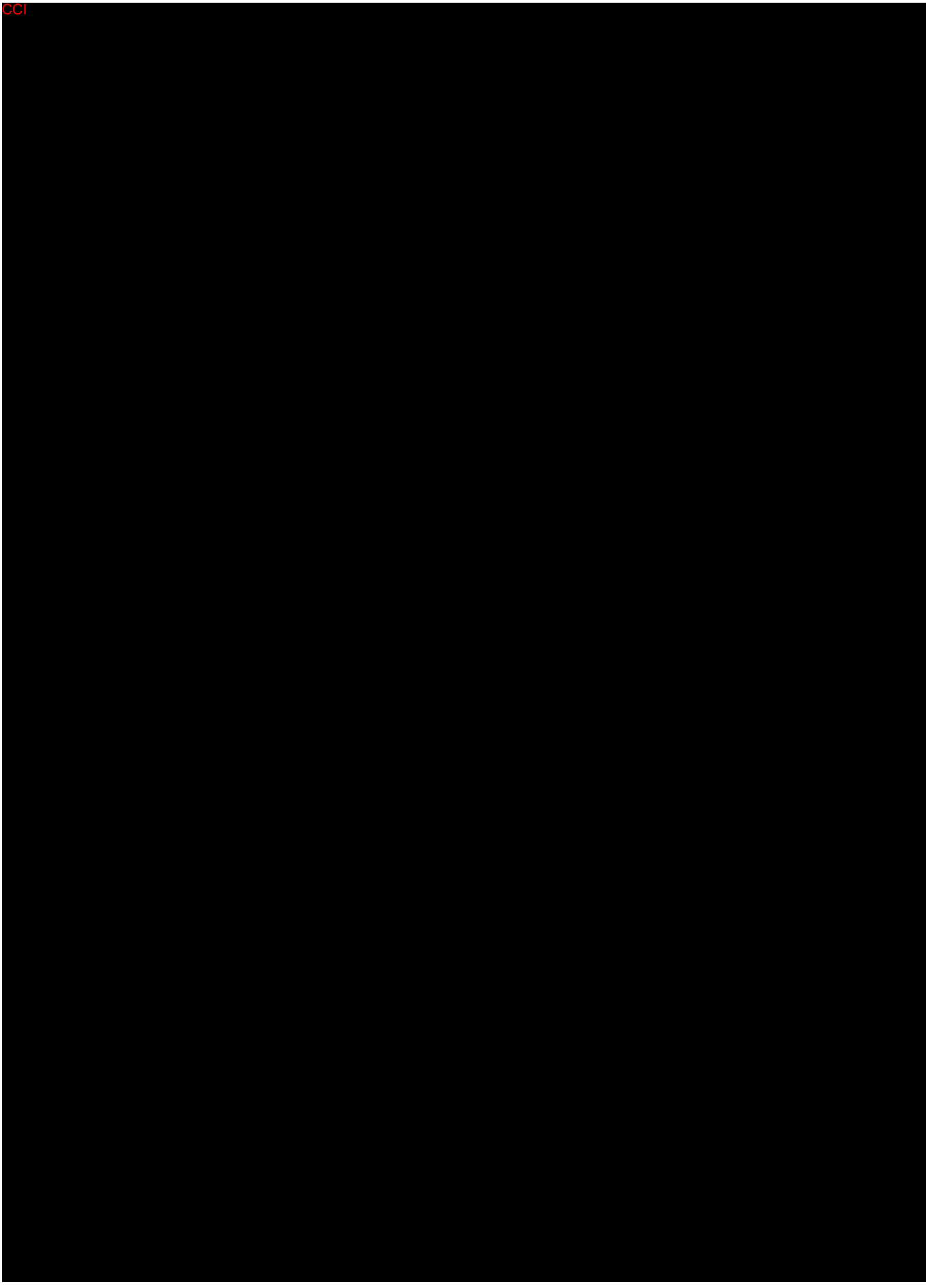
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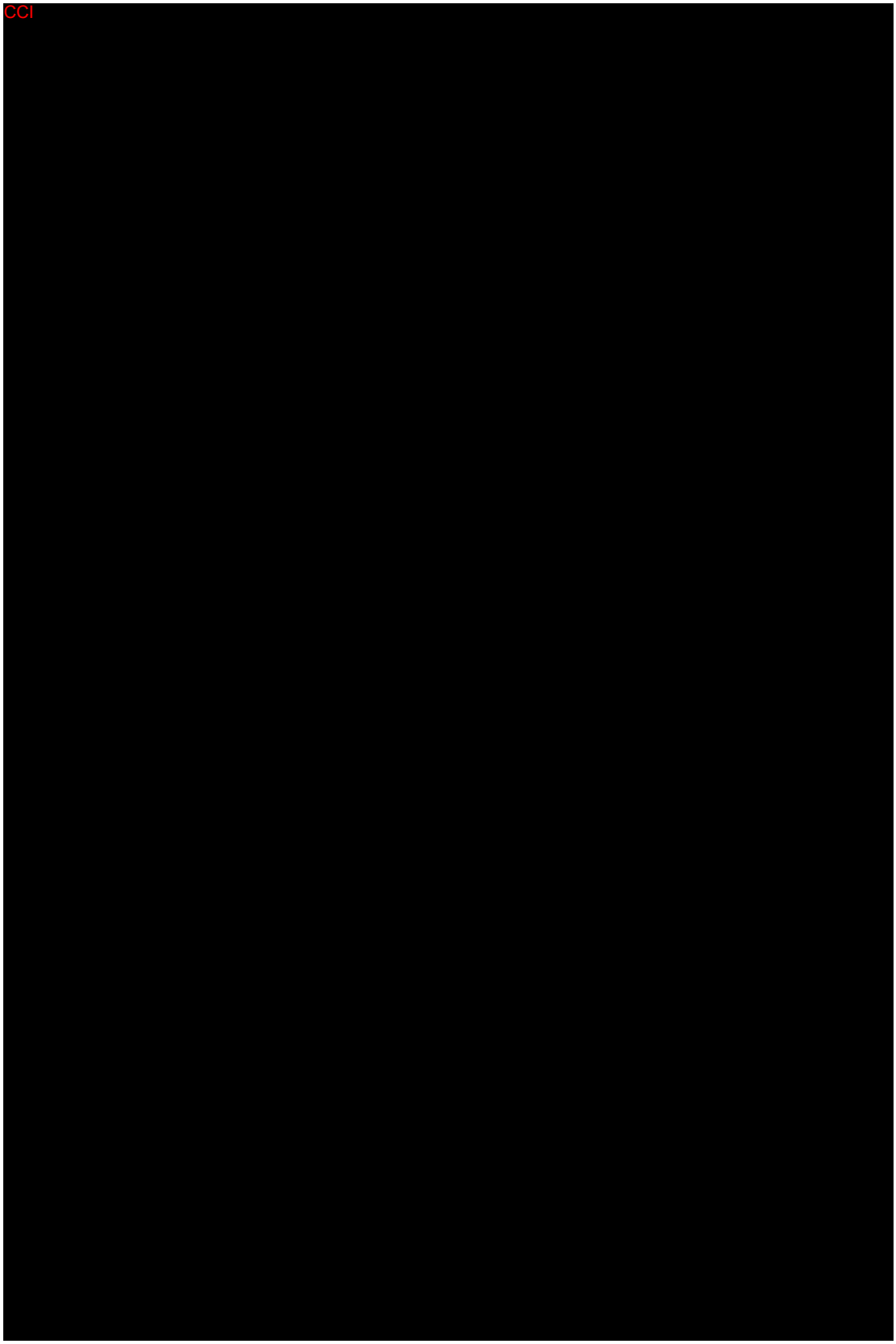

IX. Safety Analyses

The safety and tolerability of IMG-7289 will be assessed by the analysis of adverse events (AEs), as well as changes in physical examinations, vital signs, and laboratory values as detailed below, using the Safety Population.

A. Exposure

The summary will be presented by disease type (PMF, PPV-MF, and PET-MF) within the starting dose category and include the following:

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The summary by patients:

- Summary of patient weekly IMG-7289 dose during initial treatment phase

All exposure data will also be listed by starting dose category, disease type (PMF, PPV-MF, and PET-MF) and patient.

B. Adverse Events

The AEs reported on the eCRFs will be coded using the latest version of MedDRA available to the sponsor at the time of study initiation (up-versioning will not occur), associating lower-level terms with preferred terms and system organ classes (SOC) by the primary hierarchy. The tables will display counts and percentages of patients who reported at least one AE in each system organ class represented in the AE data. Within each system organ class, the tables will

display the counts and percentages of patients reporting at least one AE, as designated by the preferred terms.

In the summary, if a causal relationship is considered probable, possible, or definite by the Investigator, the AE is considered to be “related”; while, if a causal relationship is considered remote/unlikely or unrelated, the AE is considered “unrelated”.

Severity of AEs will be reported using the NCI CTCAE grades (v4.03): Grade 1 - Mild, Grade 2 - Moderate, Grade 3 - Severe, Grade 4 - Life-Threatening, and Grade 5 - Fatal.

In any given category (e.g., SOC or preferred term) a patient will be counted only once. If a patient has the same AE on multiple occasions, only the highest toxicity grade will be used. Similarly, only the most related event will be used. For summaries of related events by toxicity grade, if a patient has the same AE with both “related” and “unrelated”, only the highest toxicity grade of the related event will be used. Percentages will be based on the number of patients in the subgroup of patients being tabulated and not the number of events. Summaries that are displayed by system organ class and preferred terms will be ordered by descending order of incidence of system organ class and preferred term within each system organ class.

Sites are intended to document on the AE eCRF those events with an onset date on or after the date on which IMG-7289 was first dispensed, and within 28 days of last IMG-7289 treatment; therefore, all reported AEs are expected to be treatment-emergent. However, if eCRF completion guidelines change, or are not followed adequately, treatment-emergent events will be identified programmatically per the above definition, using imputed start date.

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C. Clinical Laboratory Results

The following laboratory tests will be conducted:

- Complete blood counts (CBC) and differential
- Coagulation
- Chemistry panel including LFTs (AST, ALT, total bilirubin and alkaline phosphatase (ALP)) gamma glutamyltransferase (GGT), albumin , C-reactive protein), lactate dehydrogenase (LDH), uric acid. *Note that C-reactive protein was added starting with amendment 5.*
- Urinalysis with microscopy

Laboratory values will be listed and summarized at each assessment. Numerical laboratory results will be summarized for the actual values, change from baseline (CFB), and percentage CFB by visit; and for the maximum and minimum change from baseline. P-value for test to assess maximum and minimum change from baseline within each cohort will be calculated using paired t-test.

Shift tables for laboratory values with respect to normal range (low, normal, high) and CTCAE toxicity grade, compared to baseline, will be summarized by visit. Overall laboratory result shift from baseline (Normal, Abnormal clinically significant (CS), and Abnormal non-clinically significant (NSC)) will be summarized.

D. Vital Signs

Vital sign assessments will be summarized for the actual values, change from baseline, and percentage change from baseline by visit; and for the maximum and minimum change from baseline. P-value for test to assess maximum and minimum change from baseline within each cohort will be calculated using paired t-test.

E. Physical Examination

Physical exam data will be listed. Note that for Phase 2b patients, a limited version of physical exam data is collected.

F. Prior and Concomitant Medications

Prior medication is defined as any medication with a stop date prior to the date of first dose of IMG-7289. Concomitant medications are defined as medications or therapies with a start date on or after the first dose of IMG-7289. Medications may be flagged as both prior and concomitant if the start date is prior to the date of the first dose of IMG-7289 and the medication continued after the first dose of IMG-7289. The medications will be coded using the most updated version of WHO Drug at the time of study initiation (up-versioning will not occur) and will be listed by cohort and by patient. The number (%) of patients using prior, prior and concomitant, and concomitant medications will be summarized.

G. Prior and Concomitant Transfusions

Prior transfusions are defined as those with a transfusion start date from the 15 days prior to Screening up to the first IMG-7289 dose. Concomitant transfusions are defined as those with a transfusion start date on or after the date of the first IMG-7289 dose. Prior and concomitant transfusions will be listed and summarized.

H. Prior and Concurrent Cancer Chemotherapy

Prior chemotherapy is defined as therapy that has ended before the first IMG-7289 dose. Concurrent cancer chemotherapy is defined as having a cancer chemotherapy start date on or after the date of the first IMG-7289 dose. Prior and concurrent chemotherapy will be listed.

X. Pharmacokinetic Analyses

Pharmacokinetic data are not within the scope of this SAP. Analysis details are provided in the protocol and in a separate Pharmacokinetic Analysis Plan.

XI. References

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