STATISTICAL ANALYSIS PLAN

Phase 1/2 Open-label, Multiple-dose, Dose-escalation Study to Evaluate the Safety and Tolerability of IMO-8400 in Patients with Relapsed or Refractory Waldenström's Macroglobulinemia

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Name of Test Drug:	IMO-8400
Phase:	Phase 1/2
Methodology:	Open-label, Multiple-dose, Dose-escalation, Multicenter
Sponsor:	Idera Pharmaceuticals, Inc. 167 Sidney Street Cambridge, MA 02139
Sponsor Representatives:	Julie Brevard, MPH Director of Statistics Idera Pharmaceuticals, Inc. Robert D. Arbeit, MD Vice President, Clinical Development Idera Pharmaceuticals, Inc.
Statistical Analysis Plan Date:	13 January 2015
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APPROVAL SIGNATURE PAGE

Protocol Title: Phase 1/2 Open-label, Multiple-dose, Dose-escalation Study to Evaluate the Safety and Tolerability of IMO-8400 in Patients with Relapsed or Refractory Waldenström's Macroglobulinemia

Sponsor: Idera Pharmaceuticals, Inc.
167 Sidney Street
Cambridge, MA 02139

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Veristat, LLC. Author:

Debora Case, MPH
Associate Biostatistician
Veristat, LLC
1750 Washington Street
Holliston, MA 01746

Signature: Debra Case

Date: 22 January 2015

Sponsor Approval

By signing this document, I acknowledge that I have read the document and approve of the planned statistical analyses described herein. I agree that the planned statistical analyses are appropriate for this study, are in accordance with the study objectives, and are consistent with the statistical methodology described in the protocol, clinical development plan, and all applicable regulatory guidances and guidelines.

I have discussed any questions I have regarding the contents of this document with the biostatistical author.

I also understand that any subsequent changes to the planned statistical analyses, as described herein, may have a regulatory impact and/or result in timeline adjustments. All changes to the planned analyses will be described in the clinical study report.

Sponsor Signatory:

Dr. Robert Arbeit
Vice President
Clinical Development
Idera Pharmaceuticals, Inc.

Signature: Robert W Arbeit MD

Date: 22 Jan 2015

Julie Brevard, MPH
Director of Statistics
Idera Pharmaceuticals, Inc.

Signature: Julie Brevard

Date: 22 JAN 2015

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Definition
AE	Adverse Event
ATC	Anatomic Therapeutic Class
BMI	Body Mass Index
CR	Complete Response
CRF	Case Report Form
CSR	Clinical Study Report
DLT	Dose Limiting Toxicity
DOR	Duration of Response
DRC	Data Review Committee
ECG	Electrocardiogram
EOS	End-of-Study
EOT	End-of-Treatment
ICH	International Conference on Harmonization
IgM	Immunoglobulin M
IRB	Institutional Review Board
ISR	Injection Site Reaction
ITT	Intent-to-Treat
MedDRA	Medical Dictionary for Regulatory Activities
MR	Minor Response
MTD	Maximum Tolerated Dose
ORR	Objective Response Rate
PD	Progressive Disease
PK	Pharmacokinetics
PP	Per Protocol
PR	Partial Response
PT	Preferred Term
Rel Day	Relative Study Day
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SC	Subcutaneous
SD	Stable Disease
SI	International System of Units
TEAE	Treatment-Emergent Adverse Event
TLR	Toll-Like Receptor
VGPR	Very Good Partial Response
WHO	World Health Organization

Abbreviation	Definition
WM	Waldenström's Macroglobulinemia

1. STATISTICAL ANALYSIS PLAN OBJECTIVES

This statistical analysis plan (SAP) is designed to outline the methods to be used in the analysis of study data in order to answer the study objectives. Populations for analysis, data handling rules, statistical methods, and formats for data presentation are provided. The statistical analyses and summary tabulations described in this SAP will provide the basis for the results sections of the clinical study report (CSR) for this trial.

This SAP will also outline any differences in the currently planned analytical objectives relative to those planned in the study protocol.

2. INFORMATION FROM THE STUDY PROTOCOL

2.1. Introduction and Objectives

2.1.1. Introduction

Waldenström's Macroglobulinemia (WM) is a distinct B-cell lymphoproliferative disorder characterized by a lymphoplasmacytic infiltrate in the bone marrow and high levels of a monoclonal immunoglobulin M (IgM) in the serum (Dimopoulos et al, 2008).The disease can have a chronic, indolent course, with patients remaining asymptomatic for years. The principal complications include manifestations of the monoclonal gammopathy, including symptomatic hyperviscosity, cryoglobulinemia, and cold agglutinin disease; disease-related cytopenia; bulky adenopathy or organomegaly; severe neuropathy; amyloidosis; and disease transformation.

Many of the agents used in refractory or relapsing WM are cytotoxic or sharply immunosuppressive and have substantial safety risks in elderly patients that are characteristic of this disease. A novel targeted agent that provided a beneficial treatment effect with a better tolerability profile would address an unmet need in WM.

IMO-8400 is a second-generation oligonucleotide antagonist of Toll-like receptors (TLR) 7, 8 and 9, which blocks immune activation mediated through those receptors. In a Phase 1 study IMO-8400 was administered to healthy adults by subcutaneous (SC) injection at single-doses and multiple-doses (once weekly for 4 weeks) up to 0.6 mg/kg (see protocol Section 5.4.1 for details). All treatments were well-tolerated, with mild injection site reactions and no pattern of systemic reactions or laboratory changes.

In recent studies, a high frequency of mutation in the signaling pathway downstream of TLR7, 8 and 9 has been identified in patients with B-cell malignancies, including more than 90% of patients with WM (Treon et al, 2012). *In vitro* studies of B-cell tumor lines indicate that such mutations are associated with an increase in cell activation, proliferation and survival (Young and Staudt, 2013), and that loss of endosomal TLRs results in markedly decreased cell proliferation and survival (Lim, Barton, and Staudt, 2013). Data from Idera indicates that treatment of such cell lines with IMO-8400 has a similar effect. Further information about the preclinical and clinical characteristics of IMO-8400 may be found in the Investigator's Brochure.

The current study represents the first clinical trial of IMO-8400 in patients with B-cell malignancy.

2.1.2. Study Objectives

2.1.2.1. Primary Objective

The primary objective is to evaluate the safety and tolerability of escalating dose levels of IMO-8400 administered by SC injection in patients with relapsed or refractory WM.

2.1.2.2. Secondary Objectives

The secondary objectives are:

- To assess the treatment effect (clinical activity) of escalating dose levels of IMO-8400 using disease-specific international guidelines for classifying clinical response (Owen et al, 2012).

- To identify an optimal dose of IMO-8400 for further clinical evaluation.
- To characterize the pharmacokinetics of escalating dose levels of IMO-8400 administered by SC injection.

2.1.2.3. Exploratory Objectives

The exploratory objectives are:

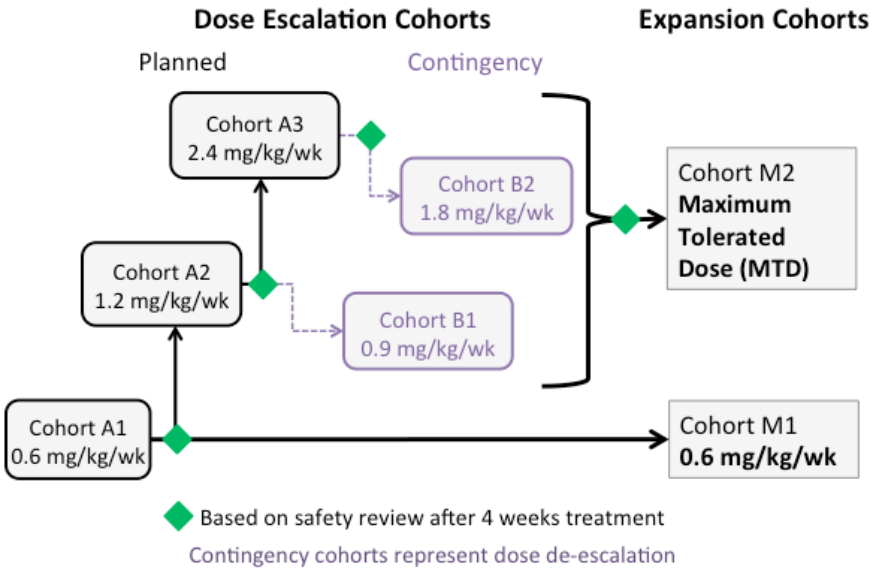
- To investigate associations between the treatment effect of IMO-8400 and selected biomarkers (e.g., serum cytokines, MyD88 L265P mutation, levels of MyD88 expression).
- To assess the potential immunogenicity of IMO-8400 administered by SC injection.

2.2. Study Design

2.2.1. Synopsis of Study Design

This is an open-label, multiple-dose, dose escalation study of IMO-8400 in patients with relapsed or refractory WM. The overall study design includes Part A, a dose escalation phase to investigate the safety and tolerability of 3 planned and 2 contingency dose levels of IMO-8400, and Part B, an expansion phase to further investigate the efficacy of the maximum tolerated dose (MTD) identified in the escalation phase (Figure 2-1).

Figure 2-1 Overall Study Design



2.2.1.1. Part A: Dose-escalation

2.2.1.1.1. Dose-escalation Cohorts

The dose-escalation cohorts (3 to 6 patients each) will systematically evaluate the safety and tolerability of IMO-8400 at increasing dose levels in order to identify the MTD. See Protocol Section 9 for further details on study treatment administration.

- The three planned dose levels are IMO-8400 at 0.6, 1.2, and 2.4 mg/kg/week (cohorts A1, A2, and A3, respectively, representing two-fold escalation). Weekly exposure is based on body weight at screening up to a maximum weekly exposure representing 125 kg equivalent.
- Provision is made for contingency cohorts at intermediate dose levels of 0.9 or 1.8 mg/kg/week (cohorts B1 and B2, respectively) to permit dose de-escalation.

Administration of the total weekly exposure will vary by dose level to facilitate giving all doses by subcutaneous injection at practical dose volumes (all <0.88 mL per injection) and solution concentrations.

- For dose levels (weekly exposures) of 0.6, 0.9, and 1.2 mg/kg, the total weekly exposure will be given as a single once weekly SC injection.
- To achieve higher weekly exposures (1.8 and 2.4 mg/kg/week), the total dose will be divided into two equal portions administered as separate subcutaneous injections (each 0.9 or 1.2 mg/kg per injection, respectively) over the course of the week, preferably 72 to 96 hours apart (minimum 48 hours).

2.2.1.1.2. Dose-escalation Procedures

Procedures for patient safety during dose-escalation are summarized below and presented in detail in the protocol sections and sections of this document indicated:

- Explicit definitions for identifying suspected adverse reactions as dose-limiting toxicity (DLT) events (see Section 2.2.5.1.1).
- Clinical or laboratory events classified Grade 3 or higher by the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), Version 4.03.
- Explicit definition for MTD (see Section 2.2.5.1.1).
- All injections of study medication will be administered by study personnel and all patients observed for 2 hours following the first injection and for at least 30 min following all other injections.
- Detailed provisions for management of study drug in individual patients based on safety, tolerability, and disease response (see Section 2.2.2.1 and Protocol Section 7.5).
- Constitution of a Data Review Committee (DRC) to make recommendations for dose-escalation and determination of the MTD (see Sections 2.2.3 and 2.2.5.1.1)

2.2.1.1.3. Dose-escalation Enrollment and Review

Each dose-escalation cohort is expected to enroll at least 3 patients, with a maximum of 6.

- If the initial 3 patients all complete 4 weeks of treatment without a DLT event, the DRC will conduct a dose-escalation review.
- If 1of the initial 3 patients experiences a DLT event prior to completing 4 weeks of treatment, then enrollment at that dose level will continue to a total of 6 patients and the dose-escalation review will be done when all 6 patients have completed 4 weeks treatment.
- If 2 patients at a dose-level experience DLT events during the first 4weeks of treatment, then no further patients will be enrolled until the DRC completes a review, which should be done as soon as feasible.

The DRC review will include all safety data available for the cohort. The following represent anticipated outcomes for the review process.

- Approve enrollment in the expansion cohort at that dose level, if applicable (See Section 2.2.1.2)
- Dose escalation – progression to the next planned dose level.
- Continue cohort enrollment (applicable only to review after three patients) – enroll up to six patients at the current dose level to obtain additional safety data for subsequent review.
- Dose de-escalation – enrollment of an intermediate level contingency cohort (see Figure 2-1) to facilitate identifying the MTD (see Section 2.2.5.1.1).
- No further dose escalation enrollment – at this time the DRC will indicate the dose level they consider represents the MTD.

2.2.1.2. Part B: Dose Expansion

2.2.1.2.1. Expansion Cohorts

The expansion cohorts provide for additional enrollment at each of 2 dose levels to assess the dose dependence of clinical response. A maximum of 9 patients may be enrolled at each specified dose level, that is, no more than 9 patients total in (a) the dose escalation cohort at that level plus (b) the corresponding expansion cohort.

- Cohort M1, 0.6 mg/kg/week
  - Expansion at this dose level will proceed only after the DRC reviews dose escalation cohort A1 (0.6 mg/kg) and concurs.
  - Patients may be enrolled in Cohort M1 while other dose escalation cohorts are proceeding. If both Cohort M1 and a dose escalation cohort are available for enrollment concurrently, the Sponsor may determine which cohort has priority.
- Cohort M2, at MTD as defined by the dose escalation process
  - Enrollment in this cohort will proceed only after the DRC either (a) determines the MTD or (b) concurs with further enrollment at 2.4 mg/kg/week, the maximum dose level under this protocol.

2.2.2. Stopping Rules

The sponsor reserves the right to discontinue the study for safety or administrative reasons at any time. Should the study be terminated and/or the site closed for whatever reason, all documentation and study medication pertaining to the study must be returned to the sponsor or its representative.

If the trial is terminated prematurely or suspended, the Sponsor will promptly inform the participating Investigators and institutions, the regulatory authorities, and the Institutional Review Board (IRB) of the termination or suspension and the reason(s) for the action.

The maximum exposures to IMO-8400, the investigational agent in this study, will be as follows:

- Maximum number of patients: 24 patients in planned escalation and expansion cohorts; potential for additional patients in contingency cohorts or as replacements
- Maximum dose level: 2.4 mg/kg/wk (two doses of 1.2 mg/kg each week)
- Maximum treatment duration: 24 weeks

2.2.2.1. Stopping Rules for Individual Patients

Each enrolled patient will receive IMO-8400 at the assigned dose level until the earliest of:

- DLT event – see Section 2.2.5.1.1
- Disease progression – based on assessments at Weeks 9 and 17, or as prompted by new signs, symptoms, and laboratory findings, and classified according to international guidelines (Owen et al, 2012) (see Sections 10.1 and 10.2 for details)
- Completion of 24 weeks treatment – Provision is made for extended treatment under a separate protocol (8400-404) at the request of the Investigator (see Protocol Section 7.5.4).

Study treatment will be discontinued for DLT clinical events and for disease progression. For DLT laboratory events, provision is made for pausing treatment for up to three weeks and, if the acute toxicity improves sufficiently, resuming treatment at a lower dose level (see Protocol Section 7.5.2 for details).

2.2.3. Data Review Committee (DRC)

Members of the DRC will have appropriate experience treating patients with hematologic malignancies and/or conducting early phase trials of investigational drugs and will include the following:

- An independent physician not otherwise involved with the study.
- The medical monitor for the study.
- A participating Investigator.
- A physician representative of the Sponsor.

The roles of the DRC are to:

- Review and provide definitive adjudication on individual DLTs (see Section 2.2.5.1.1).
- Perform dose-escalation review and make specific recommendations for the progress of the study (see Section 2.2.1.1.3).
- Determine the MTD (see Section 2.2.5.1.1).

A patient will be considered evaluable for purposes of DRC review if they meet either of the following criteria:

- Received at least one (1) dose of study drug and had treatment discontinued because of a DLT event as defined in Protocol Section 7.3.1; or
- Received four (4) doses of study drug and completed Week 5 assessment procedures.

2.2.4. Study Procedures

The schedule of assessments, as outlined in the study protocol, is provided in Table 2-2, Table 2-3, and Table 2-4.

The schedule is presented relative to the day and time of dosing. All Days are relative to the day of the first injection of study drug, designated Day 1. All weeks are relative to Week 1, defined as Day 1 through Day 7, inclusive. All times are relative to injection, designated 0 hr; "pre-dose" vital signs are to occur within 1 hour prior to injection; all other pre-dose procedures are to occur prior to injection on the same calendar day.

The screening evaluation may be performed up to 21 days prior to dosing.

Clinical and laboratory assessments for disease status will be conducted at screening, at Weeks 9 and 17 during study treatment, at the end-of-treatment (EOT) visit (week 25), and at the end-of-study (EOS) visit (week 29). Radiologic imaging and bone marrow biopsy will be performed at screening and at EOT visit. Disease status will be classified using disease-specific criteria as proposed by the VIth International Workshop on Waldenström's Macroglobulinemia (Owen et al, 2012) (see Sections 10.1 and 10.2).

In this study the duration of treatment is up to 24 weeks. This duration is consistent with the patterns of early treatment termination in the event of toxicity or disease progression with administration of investigational drugs in patients with advanced malignancies. Provision is made for extension of treatment under a separate protocol (see Protocol Section 7.5.4).

Table 2-2 Schedule of Study Events – Screening, Day 1, End-of-Treatment (EOT), End-of-Study (EOS)

Event / Visit[1]	Screen[2]	Day 1			EOT	EOS
Week			1		25[3]	29[3]
Hour		pre	0 h	post		
Informed Consent[4]	X					
Inclusion/ Exclusion Criteria	X					
Medical History	X					
Physical examination	X	X			X	X
Body weight	X[5]	X			X	X
Vital signs[6]	X	X		X[7]	X	X
Assessment of Tumor Status[8]	X				X	X
ECOG	X				X	X
CT or MRI imaging[9]	X				X	
Safety Laboratory Tests[10]	X	X			X	X
Urinalysis	X	X			X	X
12-lead ECG	X	X			X	X
Pregnancy test (females only)[11]	X				X	X
Serology	X					
Pharmacokinetics		X		X[13]	X	X
Investigational Studies[14]	X	X			X	X
Bone Marrow Biopsy[14]	X				X	
Assessment of Injection Site(s)[15]		X			X	X
Study Drug Administration			X			

AE & Concomitant Med Monitoring	------From Screening to End of Study Visit ---------

1 All Days are relative to the day of the first injection of study drug, designated Day 1. All weeks are relative to Week 1, defined as Day 1 through Day 7, inclusive. All times are relative to injection, designated 0 hr; "pre-dose" vital signs are to occur within 1 hour prior to injection; all other pre-dose procedures are to occur prior to injection on the same calendar day.
2 Screening procedures may be performed up to 21 days prior to Day 1.
3 If treatment is terminated prematurely for any reason, the EOT visit will be performed within 5 days of the decision to terminate; the EOS visit will be performed 30 to 35 days after the last dose of study drug.
4 Informed consent must be signed prior to all study-specific screening procedures.
5 At screening also height.
6 Vital signs comprise heart rate, blood pressure, respiratory rate and temperature.
7 On Day 1, post-dosing vital signs are obtained at 30 (±5) min and 2hr (±20min) after dosing.
8 Assessment of tumor status includes clinical evaluation, serum and urine levels of monoclonal protein, serum viscosity, and β2-microglobulin; see Protocol Section 10.4 for details.
9 CT or MRI imaging of chest, abdomen and pelvis with the same modality used for every assessment; see Section 10.4 for details.
10 Safety laboratory tests comprise hematology, chemistry and coagulation (see Protocol Section 10.7.1 for details).
11 Serum pregnancy testing will be done at the central laboratory.
13 At first weekly dose on Day 1, post-dose PK samples will be obtained at 1 hr (±5 min), 2 hrs (±10 min) and 4 hrs (±15 min).
14 Bone Marrow Biopsy and investigational studies will be submitted to central laboratory (see Protocol Section 10.9).
15 Assessment of all prior injection site(s) with grading and measurement of any reaction (see Protocol Section 11.4.4.2). In addition, on dosing days, the planned injection site will be assessed to confirm it is appropriate for use.

Table 2-3 Schedule of Study Events – 8-week cycles through Week 24[16]

Event / Cycle 1, Week #				2-4			5			6-8		
Cycle 2, Week #		9		10-12				13		14-16		
Cycle 3, Week #		17		18-20				21		22-24		
Hour	pre	0 h	post	pre	0 h	post	pre	0 h	post	pre	0 h	post
Informed Consent												
Medical History												
Physical examination	X			2[17]								
Body weight	X											
Vital signs[18]	X		X	X		X	X		X	X		X
Assessment of Tumor Status[19]	X											
ECOG	X											
CT or MRI imaging												
Safety Laboratory Tests[20]	X			Odd			X			Odd		
Urinalysis	X						X					
12-lead ECG	X						X					
Pregnancy test (females only)	X											
Serology												
Pharmacokinetics[21]							5,13		5,13			
Investigational Studies[22]							5,13					
Bone Marrow Biopsy												
Assessment of Injection Site(s)[23]	X			X			X			X		
Study Drug Administration[24]		X			X			X			X	

AE & Concomitant Med Monitoring	---- From Screening to End of Study Visit ----

16 All Days are relative to the day of the first injection of study drug, designated Day 1. All weeks are relative to Week 1, defined as Day 1 through Day 7, inclusive. All times are relative to injection, designated 0 hr; "pre-dose" vital signs are to occur within 1 hour prior to injection; all other pre-dose procedures are to occur prior to injection on the same calendar day.

17 Physical examination will be done on Week 2 of Cycle 1.

18 Vital signs comprise heart rate, blood pressure, respiratory rate and temperature. Post-dose vital signs are obtained at 0.5 hour after dosing.

19 Assessment of tumor status includes clinical evaluation, serum and urine levels of monoclonal protein, serum viscosity, and β2-microglobulin; see Protocol Section 10.4 for details. Samples will be collected for total and monoclonal serum IgM at Week 23 (other tumor assessments not required at Week 23).

20 The full panel of safety laboratory tests (hematology, chemistry and coagulation) will be done on Weeks 5, 9, 13, 17, and 21; a focused panel (hematology, selected chemistry) will be done on Weeks 3, 7, 11, 15, 19, and 23; see Protocol Section 10.7.1 for details).

21 PK samples will be collected on day of dosing at the first weekly dose on Weeks 5 and 13 as shown. Post-dose PK samples will be obtained at 1 hr (±5 min), 2 hrs (±10 min) and 4 hrs (±15 min) after dosing.

22 Investigational studies will be collected pre-dose at Weeks 5 and 13 (see Protocol Section 10.9 for details).

23 Assessment of all prior injection site(s) with grading and measurement of any reaction (see Section 11.4.4.2). In addition, on dosing days, the planned injection site will be assessed to confirm it is appropriate for use.

24 Schedule applies to all patients receiving once weekly dosing and to the first weekly dose for all patients receiving twice weekly dosing (see Protocol Sections 2.3.2 and 9.4 for details).

Table 2-4 Schedule of Study Events – at second weekly dosing – Weeks 1 – 24[25]

Event / All Weeks	Second Weekly Dose		
Hour	pre	0 h	post
Vital Signs[26]	X		X
Assessment of Injection Site[27]	X		
Study Drug Administration		X	

25 Schedule applies to all patients receiving ***twice*** weekly dosing. The dosing interval between the successive doses on the twice weekly schedule doses is expected to be 3 or 4 days (approximately 72 to 96 hrs), but no less than 2 days (~48 hrs) (see Protocol Sections 2.3.3and 9.4 for details). All times are relative to injection, designated 0 hr; "pre-dose" vital signs are to occur within 1 hour prior to injection; all other pre-dose procedures are to occur prior to injection on the same calendar day.

26 Vital signs comprise heart rate, blood pressure, respiratory rate and temperature. Post-dose vital signs are obtained at 30 min (± 5 min) after dosing.

27 Assessment of all prior injection site(s) with grading and measurement of any reaction (see Protocol Section 11.4.4.2). In addition, on dosing days, the planned injection site will be assessed to confirm it is appropriate for use.

2.2.5. Safety, Efficacy, and Pharmacokinetic Parameters

2.2.5.1. Safety Parameters

The safety and tolerability of IMO-8400 will be assessed using reported and observed adverse events (AEs) as well as scheduled safety observations including vital signs, physical examination, laboratory tests (hematology, chemistry, and coagulation), urinalysis, and electrocardiograms (ECGs).

Adverse Events will be coded using Medical Dictionary for Regulatory Activities (MedDRA) version 16.0 and tabulated by event, grade, and relationship to study therapy. Laboratory results, vital signs, and ECG parameters will be summarized using descriptive statistics. Laboratory values will also be graded according to NCI CTCAE, Version 4.03, and summarized using shift tables.

2.2.5.1.1. Definition of Dose Limiting Toxicity and Maximum Tolerated Dose

A DLT can be either a clinical or laboratory AE. A potential DLT event is defined as a treatment-emergent (i.e. onset after first injection of study drug) AE that meets *either* of the following criteria using NCI CTCAE v4.03 grading:

- Is a clinical event of Grade 3 or higher severity.
- Is a confirmed laboratory finding of Grade 3 or higher severity.

The DRC will review all potential DLT events to assess causality, i.e., relationship to study drug (related, possible related, unlikely related, or not related). Events will be considered DLT events unless they are unanimously assessed as “Not related”, that is, a factor other than study drug is the cause of the event.

The MTD is the dose level meeting *both* of the following criteria:

- It is below the level at which 2 or more patients experienced DLTs during the first four weeks of treatment;
- It is a dose level at which no more than 1 patient experienced DLTs during the first four weeks of treatment.

2.2.5.2. Efficacy Parameters

The primary treatment effect parameter is objective response rate (ORR), defined as the occurrence of complete response (CR), very good partial response (VGPR), partial response (PR), or minimal response (MR), presented by dose level and overall.

Secondary efficacy endpoints include:

- The distribution of response classes identified by best overall response.
- Duration of response (DOR) – Time from the first occurrence of objective response (CR, VGPR, PR, or MR) to the first documented evidence of disease progression.
- Time to progression (TTP) – Time from the initiation of treatment to disease progression with deaths due to unrelated causes censored.
- Progression-free survival (PFS) – Time from the initiation of treatment to disease progression or death from any cause.

- Time to best observed response – Time from the initiation of treatment to best observed category of response
- Percent and absolute change in quantitative serum levels of monoclonal IgM.
- Percent and absolute change in hematology values (if abnormal at baseline).

Exploratory endpoints include the following investigational factors, analyzed with regard to disease status:

- Presence or absence of MyD88 L265P mutation in tumor cells.
- Serum cytokine levels.
- Serum levels of antibody to IMO-8400.

Additional exploratory analysis may be performed on additional endpoints of interest or subpopulations.

2.2.5.3. Pharmacokinetic Parameters

Blood samples for plasma levels of IMO-8400 will be collected as scheduled. Samples will be analyzed for IMO-8400 concentration using a ligand binding (hybridization) bioanalytical method (estimated sensitivity, 20 ng/mL). Pharmacokinetic data will be analyzed using standard non-compartmental methods.

The pharmacokinetic variables to be determined and the time points of determination are summarized below:

Table 2-5 Pharmacokinetic Parameters for Analysis

Parameter	Description	Equation
$AUC_{0\text{-last}}$	Area-under-the-curve from 0 to last measurable concentration	
C_{max}	Maximum plasma concentration; the highest concentration observed during a dosage interval.	
T_{max}	The time C_{max} was observed.	
R_A	Accumulation Ratio: Ratio of drug concentrations observed during a dosing interval at steady-state divided by drug concentrations seen during the dosing interval after a single (first) dose	$AUC_{0\text{-last}}$ - multiple dose / $AUC_{0\text{-last}}$ - single (first) dose

3. SUBJECT POPULATION

3.1. Population Definitions

The following subject populations will be evaluated and used for presentation and analysis of the data:

Intent-to-Treat (ITT)/Safety Population: All patients who received at least one dose of study treatment.

Per Protocol (PP) Population: All patients who have one or more scheduled post-treatment tumor assessments and no major protocol deviations.

Pharmacokinetic (PK) Population: All patients with sufficient data to determine PK parameters.

The primary efficacy endpoint (objective response rate) will be analyzed for both ITT/Safety and PP populations. Secondary and exploratory efficacy endpoints will be analyzed using only PP population, with the exception of several key secondary efficacy endpoints, which will be analyzed for the ITT/Safety population as well.

The ITT/Safety population is the primary population for the analysis of safety parameters. The PK population is the primary population for the analysis of PK parameters.

3.2. Protocol Deviations

For protocol deviations relating to individual patients, the event and relevant circumstances will be recorded on source documents and on the appropriate eCRF. Protocol deviations will be determined and documented prior to database lock. Upon assessment of protocol deviations, the Sponsor may determine to remove a patient's data from the PP population in an effort to maintain full compliance with study procedures.

All protocol deviations will be presented in a data listing.

Relevant Output

Listing 16.2.3 Protocol Deviations

4. GENERAL STATISTICAL METHODS

4.1. Sample Size Justification

Consistent with the primary objective, the study design represents a pragmatic assessment of safety and tolerability across different dose levels of IMO-8400 based upon clinical evaluations and laboratory tests.

It is anticipated that there will be sufficient patients to permit a preliminary evaluation of treatment effect at the expansion dose levels (see Section 2.2.1.2) and globally across dose levels.

A power calculation relating to the primary treatment effect analysis was performed using the following assumptions:

- 9 patients at an expansion dose level or 18 patients across the two expansion dose levels.
- True response rate at least 50%.
- Using a one-sided exact test and significance level $\alpha = 0.025$.
- A hypothetical response rate of 10%.

Under these assumptions, 9 patients will provide at least 74% power for rejecting the hypothetical response rate; and 18 patients will provide at least 96% power.

4.2. General Methods

All data listings that contain an evaluation date will contain a relative study day (Rel Day). For the purpose of analysis, study days will be designated as follows:

- Day 1 is defined as the calendar day of the first injection of study drug.
- The days prior to Day 1 are designated Day –1, Day –2, etc; there is no Day 0.
- The days following the day of the first injection of study drug are designated Day 2, Day 3, etc.
- The day of the last injection of study drug is indicated by adding the suffix "L", e.g., if the last injection is administered on Day 43, it will be displayed as "Day 43L".
- The days following the last injection of study drug are designated Day 1P, Day 2P, etc.
- The times of events related to dosing of study drug will be designated as minutes or hours before or after the time of dosing (i.e., the subcutaneous injection of study drug), which is designated as t = 0 (zero). Thus, 15 minutes prior to dosing is t = –15 min; 2 hour after dosing is designated t = 2 h.

All output will be incorporated into Microsoft Word files, sorted and labeled according to the International Conference on Harmonisation (ICH) recommendations, and formatted to the appropriate page size(s).

Tabulations will be produced for appropriate demographic, baseline, efficacy, PK, and safety parameters. For categorical variables, summary tabulations of the number and percentage of patients within each category (with a category for missing data) of the parameter will be presented. For continuous variables, the number of patients, mean, median, standard deviation, minimum, and maximum values will be presented. For some efficacy parameters, a confidence interval will also be presented, as described in more detail in Section 5.

Data will be presented by subject and summarized by dose and overall, including a pooled cohort of all IMO-8400 dosed groups. All data will be included in summary tabulations..

4.3. Computing Environment

All descriptive statistical analyses will be performed using SAS statistical software Version 9.3 or above, unless otherwise noted. Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) Version 16.0 (or later). Concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary Version Q12013 (or later).

4.4. Baseline Definitions

For all analyses, baseline will be defined as the most recent measurement prior to the first administration of study drug.

4.5. Methods of Pooling Data

Data will be pooled across all study sites. All IMO-8400 dosed subjects will be pooled together and presented separately by dose level.

4.6. Adjustments for Covariates

In an exploratory efficacy analysis for all efficacy endpoints, the presence or absence of the MyD88 L265P mutation may be included in the model as a covariate.

4.7. Multiple Comparisons

No adjustments for multiple comparisons will be made. As the primary purpose of this study is to assess the safety and tolerability of IMO-8400, efficacy assessments are secondary and the type I error rate will not be adjusted.

4.8. Subpopulations

In an exploratory efficacy analysis, all efficacy endpoints will be repeated by MyD88 L265P mutation status subpopulation (i.e., those with and without the mutation as measured at baseline).

4.9. Withdrawals, Dropouts, Loss to Follow-up

A patient who does not meet the criteria for "evaluable" as explained above in Section 2.2.3 may be replaced to assure the requirements for completing the cohort are met. Replacement patients will be identified by distinctive patient numbers and will receive the same dose level as the patient being replaced.

4.10. Missing, Unused, and Spurious Data

Missing data will not be imputed. All the data recorded on the case report form (CRF) will be included in data listings that will accompany the CSR.

When tabulating AE data, partial dates will be handled as follows. If the day of the month is missing, the onset day will be set to the first day of the month unless it is the same month and year as study treatment. In this case, in order to conservatively report the event as treatment-emergent, the onset date will be assumed to be the first date of treatment. If the onset day and month are both missing, the day and month will be assumed to be January 1, unless the event occurred in the same year as the study treatment. In this case, the event onset will be coded to the day of treatment in order to conservatively report the event as treatment-emergent. A

missing onset date will be coded as the first day of treatment. Listings will present all data as reported (i.e., without imputations).

4.11. Visit Windows

It is expected that all visits should occur according to the protocol schedule; visits outside of this schedule will be listed as a protocol deviation. Visits occuring outside of the visit windows as described in the protocol schedule will be included in summary tabulations if corresponding to a scheduled visit. Unscheduled assessments will not be summarized in tabulations that present data by visit. However, in shift tables or summaries of best response, data from unscheduled assessments will be included. Any data from unscheduled assessments will be listed.

In data listings, the relative day of all dates will be presented.

4.12. Interim Analyses

Interim safety data will be examined on an ongoing basis to ensure patient safety and to comply with the clinical trial dose escalation rules. There is no formal interim analysis planned for efficacy.

5. STUDY ANALYSES

5.1. Patient Disposition

Patient disposition will be tabulated and will include the number screened, the number screen failed, the number enrolled, the number treated at each dose level, the number prematurely discontinued from treatment, the reason for discontinuation, and the number in each subject population for analysis. The definitions of the parameters used in the disposition table are given below.

Screened: Patients who signed consent and underwent screening procedure.

Screen Failure: Screened patients deemed ineligible to enroll in the study due to failure to meet the inclusion/exclusion criteria.

Enrolled: Patients who received at least 1 dose of study medication.

A by-subject data listing of study completion information including the reason for premature study withdrawal and premature treatment discontinuation will be presented. A by-patient data listing of inclusion/exclusion criteria not met and will also be presented.

Relevant Output

Table 14.1.1.1	Patient Enrollment and Disposition
Listing 16.2.1.1	Patients Discontinuing Treatment Prematurely
Listing 16.2.1.2	End of Treatment (EOT) Visit Status
Listing 16.2.1.3	End of Study (EOS) Visit Status
Listing 16.2.2.1	Inclusion Criteria
Listing 16.2.2.2	Exclusion Criteria
Listing 16.2.2.3	Listing of Inclusion/Exclusion Criteria Not Met
Listing 16.2.2.4	Intent–To-Treat Patients Excluded from Per-Protocol Population

5.2. Demographics and Baseline Characteristics

Demographics and baseline characteristics, including medical and disease history, will be summarized and presented by dose level and overall. Age, height, weight, body mass index (BMI), and baseline ECOG Score will be summarized using descriptive statistics (number of patients, mean, standard deviation, median, minimum, and maximum). The number and percentage of patients in each ethnicity, race and gender category will also be presented.

Disease history will include number and percentage of subjects with presence or absence of MyD88 L265P mutation in tumor cells, whether at least one treatment related AE has been recorded in the past 3 months, and whether the subject has been hospitalized in the past year. Time since WM diagnosis, time since first treatment for WM, and time since most recent hospitalization will be summarized using descriptive statistics.

Prior treatments will include number and percentage of patients who have received at least one prior therapy, including type of treatment and best overall response.

Demographic, baseline, and medical history data for each subject will be provided in data listings.

Relevant Output

Table 14.1.2.1	Demographic Characteristics (ITT/Safety Population)
Tabel 14.1.2.2	Baseline Characteristics (ITT/Safety Population)
Table 14.1.3.1	Disease History (ITT/Safety Population)
Table 14.1.4.1	Prior Treatments (ITT/Safety Population)
Listing 16.2.4.1	Demographic Characteristics
Listing 16.2.4.2	Medical History
Listing 16.2.4.3A	Waldenström's Macroglobulinemia Disease History – Part 1
Listing 16.2.4.3B	Waldenström's Macroglobulinemia Disease History – Part 2
Listing 16.2.4.4	Prior Waldenström's Macroglobulinemia Therapy
Listing 16.2.8.6	Urine Pregnancy Test Results
Listing 16.2.9.3	Eastern Cooperative Oncology Group (ECOG) Performance Status

5.3. Safety Analyses

Safety analyses will be conducted using the Safety population. Safety observations will be analyzed using descriptive statistics and tabulation. No formal statistical comparisons are planned. All safety data will be presented in listings.

5.3.1. Study Drug Exposure

Study drug exposure will be tabulated by the number of cycles of study drug received. The number and percentage of patients will be reported by dose group and overall. Cumulative dose (mg) will also be summarized by dose group and overall, where cumulative dose is the dose injected multiplied times the number of injections, taking into account any intrapatient dose adjustments. The number of missed doses will also be tabulated, as well as the reason the dose was missed. Dosing information for each subject will be presented in a data listing.

Relevant Output

Table 14.3.5.1	Study Drug Exposure (ITT/ Safety Population)
Table 14.3.5.2	Study Drug Exposure (PP Population)
Listing 16.2.5.1	Study Drug Exposure

5.3.2. Adverse Events

Adverse events will be coded using the MedDRA coding system and displayed in tables and data listings using system organ class (SOC) and preferred term.

Analyses of AEs will be performed for those events that are considered treatment-emergent, where treatment-emergent is defined as:

- any AE with onset after the first administration of study medication (Day 1) through the EOS visit,
- any AE that was present at baseline but worsened in intensity or was subsequently considered drug-related by the Investigator through the EOS visit, or
- any AE with missing onset date.

The incidence of AEs will be presented by individual and pooled dose levels. For each tabulation, AEs are summarized by subject incidence rates; therefore, in any tabulation, a subject contributes only once to the count for a given AE (SOC or preferred term), irrespective

of the number of episodes of a particular AE term reported. No formal hypothesis-testing analysis of AE incidence rates will be performed.

The number and percentage of patients with any AE, injection site reaction (ISR), treatment-emergent AE (TEAE), TEAE related to study drug, grade ≥3 TEAE, serious AE (SAE) and DLT AE will be presented.

Additional summary tables by SOC and preferred term will be produced for the following:

- All TEAEs
- All TEAEs by relationship to study drug (drug-related, not drug-related) where drug-related AEs include events with probable, possible and missing relationships
- All non-serious TEAEs
- All TEAEs by severity grade (grade 1 or 2, grade ≥3)
- All DLTs

For each injection site, local ISRs will be summarized by the worst grade post-treatment for each symptom. Pain, tenderness, pruritus and induration will be summarized using number and percentage of patients by toxicity grade. Blisters, ulceration and necrosis measurements (mm) will be summarized descriptively, including quartiles and 90^{th} percentiles, as well as categorically by grade. For each injection site the worst grade post treatment is counted per subject and symptom. In addition, each symptom will be summarized over time by visit and grade.

All AEs occurring on-study will be listed in subject data listings. Additionally, a glossary of AE verbatim terms by preferred term and SOC will be provided. A separate listing for system organ class complete name and their corresponding abbreviations will be provided.

By-subject listings will also be provided for the following: subject deaths, SAEs, and AEs leading to withdrawal.

Relevant Output

Table 14.3.1.1	Summary of Adverse Events (ITT/ Safety Population)
Table 14.3.1.2	Incidence of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term (ITT/ Safety Population)
Table 14.3.1.3	Incidence of Treatment-Emergent Adverse Events by Relationship to Study Drug and by MedDRA System Organ Class and Preferred Term (ITT/ Safety Population)
Table 14.3.1.4	Incidence of Non-Serious Adverse Events, by MedDRA System Organ Class and Preferred Term (Safety Population)
Table 14.3.1.5	Incidence of Treatment-Emergent Adverse Events by Intensity and by MedDRA System Organ Class and Preferred Term (ITT/ Safety Population)
Table 14.3.1.6	Incidence of Dose-Limiting Toxicity Adverse Events by MedDRA System Organ Class and Preferred Term (ITT/ Safety Population)
Table 14.3.1.7	Incidence of Local Injection Site Reactions Worst Grade Post Baseline (ITT/ Safety Population)
Table 14.3.1.8	Incidence of Local Injection Site Reactions Worst Grade by Visit (ITT/ Safety Population)
Table 14.3.2.1	Listing of Deaths
Table 14.3.2.2	Listing of Serious Adverse Events
Table 14.3.2.3	Listing of Treatment Discontinuations Due to Adverse Events

Listing 16.0.1	System Organ Class Abbreviations
Listing 16.2.7.1	Adverse Events by Patient and System Organ Class / Preferred Term
Listing 16.2.7.2	Adverse Events by System Organ Class / Preferred Term
Listing 16.2.7.3	Glossary of Adverse Event Verbatim Terms by MedDRA System Organ Class, Preferred Term, and Patient
Listing 16.2.7.4	Injection Site Reaction Assessments
Listing 16.2.7.5	Patient Reported Injection Site Reactions
Listing 16.2.7.6	Observed Injection Site Reactions

5.3.3. Laboratory Data

Clinical laboratory values will be reported in US units.

This study collects central laboratory data, but local laboratory data may be collected for the screening visit. Local laboratory data will not be summarized but it will be included in the laboratory listings.

The actual value and change from baseline to each on-study evaluation will be summarized for hematology, chemistry and coagulation parameters. A boxplot figure representing each lab parameter over time will be presented for hematology, chemistry and coagulation parameters by dose level and overall.

Laboratory CTCAE grades shift from baseline to the worst grade post baseline will be tabulated for individual and pooled dose groups using number and percentage of patients. These comparisons will include values from unscheduled visits.

All laboratory data will be provided in data listings. A separate listing including normal ranges for all hematology, chemistry, coagulation and urinalysis parameters will be provided.

A subset listing will be presented for all clinically significant and abnormal laboratory values.

Relevant Output:

Table 14.3.4.1	Listing of Clinically Significant Abnormal Laboratory Values (ITT/ Safety Population)
Table 14.3.5.3	Summary and Change from Baseline for Hematology Parameters by Time Point and Dose Group (ITT/ Safety Population)
Figure 14.3.5.3	Summary and Change from Baseline for Hematology Parameters by Time Point and Dose Group - Box Plot (ITT/ Safety Population)
Table 14.3.5.4	Summary and Change from Baseline for Chemistry Parameters by Time Point and Dose Group (ITT/ Safety Population)
Figure 14.3.5.4	Summary and Change from Baseline for Chemistry Parameters by Time Point and Dose Group - Box Plot (ITT/ Safety Population)
Table 14.3.5.5	Summary and Change from Baseline for Coagulation Parameters by Time Point and Dose Group (ITT/ Safety Population)
Figure 14.3.5.5	Summary and Change from Baseline for Coagulation Parameters by Time Point and Dose Group - Box Plot (ITT/ Safety Population)
Table 14.3.5.6A	Shifts from Baseline to Worst CTC Grade Post-Baseline in Hematology Parameters by Dose Group (ITT/ Safety Population)
Table 14.3.5.6B	Shifts from Baseline to Worst CTC Grade Post-Baseline in Chemistry Parameters by Dose Group (ITT/ Safety Population)
Table 14.3.5.6C	Shifts from Baseline to Worst CTC Grade Post-Baseline in Coagulation Parameters by Dose Group (ITT/ Safety Population)

Listing 16.2.8.1A Laboratory Results: Hematology – Part 1
Listing 16.2.8.1B Laboratory Results: Hematology – Part 2
Listing 16.2.8.2 Laboratory Results: Chemistry
Listing 16.2.8.3 Laboratory Results: Urinalysis
Listing 16.2.8.4 Laboratory Results: Coagulation

5.3.4. Vital Signs

The actual value and change from baseline to each on-study evaluation will be summarized for vital signs, including heart rate, blood pressure, respiratory rate, and temperature. A boxplot figure representing each vital sign over time will be presented by dose group and overall.

Vital sign measurements will be presented in a data listing.

Relevant Output:

Table 14.3.5.7 Summary and Change from Baseline for Vital Signs by Time Point and Dose Group (ITT/Safety Population)
Figure 14.3.5.7 Summary and Change from Baseline for Vital Signs by Time Point and Dose Group - Box Plot (ITT/Safety Population)

Listing 16.2.9.1 Vital Signs

5.3.5. Physical Examination

All physical examination findings will be presented in a data listing.

Relevant Output:

Listing 16.2.9.2 Physical Examination Findings

5.3.6. Electrocardiogram

Actual ECG values and change from baseline will be summarized descriptively by time point, including heart rate and PR, QRS, QT, and QTcF (calculated by the Fridericia correction formula).

Electrocardiogram data will be provided in a data listing.

Relevant Output:

Table 14.3.5.8 Summary and Change from Baseline for Electrocardiogram Results by Time Point and Dose Group (ITT/Safety Population)
Table 14.3.5.9 Listing of Abnormal Electrocardiogram Assessments (ITT/Safety Population)

Listing 16.2.9.4 12-Lead Electrocardiogram Interval and Overall Assessment
Listing 16.2.9.5 12-Lead Electrocardiogram – Comments on Abnormal Assessments

5.3.7. Concomitant Medications

Concomitant medications will be coded using the WHO Drug Dictionary. Results will be tabulated by anatomic therapeutic class (ATC) and preferred term.

Any medications that did not end prior to first dose will be classified as a concomitant medication, as well as medications that are ongoing or those missing the end date. In case of

repeated occurrences per subject, a medication will only be counted once per ATC/preferred term.

The use of concomitant medications will be included in a by-subject data listing.

Relevant Output:

Table 14.3.5.10 Concomitant Medications (Safety Population)

Listing 16.2.9.6 Concomitant Medications

5.4. Efficacy Analyses

Study populations for the primary, secondary and supplemental efficacy analysis are defined in Section 3.1. The primary efficacy endpoint will be analyzed for both ITT and PP populations. Secondary and exploratory efficacy endpoints will be analyzed using only ITT population, unless the difference in number of patients between ITT and PP populations is >2, in which case the analyses will be performed using both ITT and PP populations.

For patients who discontinue study treatment for any reason and start another treatment of their malignancy, all subsequent response assessments from the date of start of another treatment will be excluded from the analysis.

5.4.1. Primary Efficacy Analysis

The primary statistical analysis of efficacy will be performed on the objective response rate (ORR). The ORR will be presented by dose level and overall with corresponding 90% confidence intervals (CIs) using the Wilson method.

Relevant Output

Table 14.2.1.1.1 Objective Response Rate Primary Efficacy Analysis (ITT/Safety Population)
Table 14.2.1.1.2 Objective Response Rate Primary Efficacy Analysis (PP Population)

Listing 16.2.6.1 Disease Response
Listing 16.2.6.2A Disease Assessment – Part 1
Listing 16.2.6.2B Disease Assessment – Part 2

5.4.2. Secondary Efficacy Analyses

The following parameters will be analyzed by dose level and overall. Time-to-event analyses will use the Kaplan- Meier (KM) method for estimation of summary statistics, and include the 25th, 50th (median) and 75th percentiles, associated 90% CIs on the median and other percentiles, and proportion of censored subjects. A corresponding KM curve will be presented for each time-to-event parameter.

- Best overall response. The number and percentage of subjects in each response category will be summarized.
- Duration of objective response (DOR) – Number of days from the first occurrence of objective response to the first documented evidence of disease progression. Subjects who have not progressed prior to the data cut-off for final efficacy analysis, who drop out prior to study end, or who pass away prior to documentation of disease progression will be censored at the date of the last valid disease assessment. The DOR analysis will use the KM method as described above.
- Time to progression (TTP) – Number of days from the initiation of treatment to disease progression with deaths due to unrelated causes censored at the date of the last valid disease

assessment. Subjects who have not progressed prior to the data cut-off for final efficacy analysis, or who drop out prior to study end, will be censored at the date of the last valid disease assessment. The TTP analysis will use the KM method as described above.

- Progression-free survival (PFS) – Number of days from the initiation of treatment to disease progression or death from any cause. Subjects who have not progressed prior to the data cut-off for final efficacy analysis, or who drop out prior to study end, will be censored at the date of the last valid disease assessment. The PFS analysis will use the KM method as described above.
- Time to best observed response – Number of days from the initiation of treatment to best observed category of response. Patients who do not have a response recorded will be censored at date of first treatment dose. The time to best observed response analysis will use the KM method as described above.
- Percent and absolute change in quantitative serum levels of total IgM. - Descriptive statistics, including change over time will be presented by dose group and overall. A figure representing mean value will be presented with standard deviation as error bars will also be presented.

A repeated measures mixed model will be performed for the change in quantitative serum levels of total IgM. The model will include dose group, study day, the interaction of dose group and study day, baseline value of the respective outcome variable and MyD88 mutation status as independent variables. Parameters will initially be analyzed without transformation, but if the data suggest otherwise, log transformation may be applied. The data will be examined by the statistician to identify the shape of the relationship between dose and time and the model may be adjusted accordingly. This may include treatment of time as a categorical or continuous variable, adding a quadratic term to the model, etc. In the case that the interaction between dose group and study day is not statistically significant at the one-sided 0.10 level, the interaction may be excluded from the model.

The treatment effect will be reported for each dosing cohort including the least square mean estimates and the 90% confidence interval. If the overall test for treatment effect is statistically significant at the one-sided 0.10 level, pairwise comparisons will be performed using one-sided type I error rates of 0.10 for each comparison. Graphs of the least square mean estimates over time will be presented with standard error as error bars.

Relevant Output

Table 14.2.1.2.1	Best Overall Response Secondary Efficacy Analysis (ITT/Safety Population)
Table 14.2.1.2.2	Best Overall Response Secondary Efficacy Analysis (PP Population)
Table 14.2.1.3.1	Duration of Objective Response Secondary Efficacy Analysis (PP Population)
Figure 14.2.1.3.1	Duration of Objective Response Secondary Efficacy Analysis Kaplan-Meier Curve (PP Population)
Table 14.2.1.4.1	Time to Progression Secondary Efficacy Analysis (ITT/Safety Population)
Figure 14.2.1.4.1	Time to Progression Secondary Efficacy Analysis Kaplan-Meier Curve (ITT/Safety Population)
Table 14.2.1.4.2	Time to Progression Secondary Efficacy Analysis (PP Population)
Figure 14.2.1.4.2	Time to Progression Secondary Efficacy Analysis Kaplan-Meier Curve (PP Population)
Table 14.2.1.5.1	Progression-Free Survival Secondary Efficacy Analysis (PP Population)
Figure 14.2.1.5.1	Progression-Free Survival Secondary Efficacy Analysis Kaplan-Meier Curve (PP Population)

Table 14.2.1.6.1	Time to Best Observed Response Secondary Efficacy Analysis (PP Population)
Figure 14.2.1.6.1	Time to Best Observed Response Secondary Efficacy Analysis Kaplan-Meier Curve (PP Population)
Table 14.2.3.1.1	Percent Change from Baseline in Quantitative Serum Levels of Total IgM (ITT/Safety Population)
Figure 14.2.3.1.1	Percent Change from Baseline in Quantitative Serum Levels of Total IgM Box Plot (ITT/Safety Population)
Table 14.2.3.1.2	Percent Change from Baseline in Quantitative Serum Levels of Total IgM (PP Population)
Figure 14.2.3.1.2	Percent Change from Baseline in Quantitative Serum Levels of Total IgM Box Plot (PP Population)
Table 14.2.3.2.1	Change from Baseline in Quantitative Serum Levels of Total IgM (ITT/Safety Population)
Figure 14.2.3.2.1	Change from Baseline in Quantitative Serum Levels of Total IgM Box Plot (ITT/Safety Population)
Table 14.2.3.2.2	Change from Baseline in Quantitative Serum Levels of Total IgM (PP Population)
Figure 14.2.3.2.2	Change from Baseline in Quantitative Serum Levels of Total IgM Box Plot (PP Population)
Table 14.2.5.1.1	Change in Quantitative Serum Levels of Total IgM – Repeated Measures Analysis (ITT/Safety Population)
Table 14.2.5.1.2	Change in Quantitative Serum Levels of Total IgM – Repeated Measures Analysis (PP Population)
Table 14.2.5.2.1	Change in Quantitative Serum Levels of Total IgM – Repeated Measures Analysis Least Square Means by Visit (ITT/Safety Population)
Figure 14.2.5.2.1	Change in Quantitative Serum Levels of Total IgM - Repeated Measures Analysis: Least Square Means over Time (ITT/Safety Population)
Table 14.2.5.2.2	Change in Quantitative Serum Levels of Total IgM – Repeated Measures Analysis Least Square Means by Visit (PP Population)
Figure 14.2.5.2.2	Change in Quantitative Serum Levels of Total IgM - Repeated Measures Analysis: Least Square Means over Time (PP Population)
Listing 16.2.6.1	Disease Response
Listing 16.2.6.2A	Disease Assessment – Part 1
Listing 16.2.6.2B	Disease Assessment – Part 2
Listing 16.2.8.9	Immunoglobin (IgM) Results

5.4.3. Exploratory Analyses

The following investigational factors will be analyzed with regard to disease status and presented both globally across all cohorts and by dose level.

- Presence or absence of MyD88 L265P mutation in tumor cells – Selected efficacy analyses described above will be repeated by mutation status subpopulation.
- Serum cytokine levels - Descriptive statistics, including change over time will be presented by visit.
- Serum levels of antibody to IMO-8400 – Number and percent of subjects with antibody present will be presented by visit.

Additional exploratory analysis may occur.

Relevant Output

Table 14.2.2.1.1	Objective Response Rate Primary Efficacy Analysis by MyD88 Mutation Status (ITT/Safety Population)
Table 14.2.2.1.2	Objective Response Rate Primary Efficacy Analysis by MyD88 Mutation Status (PP Population)
Table 14.2.2.2.1	Best Overall Response Secondary Efficacy Analysis by MyD88 Mutation Status (PP Population)
Table 14.2.2.4.1	Time to Progression Secondary Efficacy Analysis by MyD88 Mutation Status (PP Population)
Figure 14.2.2.4.1	Time to Progression Secondary Efficacy Analysis by MyD88 Mutation Status Kaplan-Meier Curve (PP Population)
Table 14.2.4.1.1	Percent Change from Baseline in Quantitative Serum Levels of Total IgM by MyD88 Mutation Status (PP Population)
Figure 14.2.4.1.1	Percent Change from Baseline in Quantitative Serum Levels of Total IgM by MyD88 Mutation Status Box Plot (PP Population)
Table 14.2.4.2.1	Change from Baseline in Quantitative Serum Levels of Total IgM by MyD88 Mutation Status (PP Population)
Figure 14.2.4.2.1	Change from Baseline in Quantitative Serum Levels of Total IgM by MyD88 Mutation Status Box Plot (PP Population)
Listing 16.2.4.5	MyD88 L265P Mutation Status
Listing 16.2.8.8	Serum Cytokines Test
Listing 16.2.8.10	Serum Antibody Results

5.5. Pharmacokinetic Analyses

Pharmacokinetic analyses will be conducted using the PK population.

Blood samples for plasma levels of IMO-8400 will be collected as scheduled. Samples will be analyzed for IMO-8400 concentration using a ligand binding (hybridization) bioanalytical method (estimated sensitivity, 20 ng/mL). Pharmacokinetic data will be summarized descriptively by dose group and overall.

Plasma concentrations below the limit of quantification (BQL) will be assigned a value of zero when they precede the first quantifiable sample. Any BQL values embedded between 2 quantifiable data points will be treated as missing. Missing values will not be imputed, and if sufficient data are missing for a given subject, that subject may be considered non-evaluable for pharmacokinetic analysis.

Summary statistics will be provided for each of these PK parameters by dose group and overall. The geometric mean and %CV will be presented for $AUC_{0\text{-last}}$, C_{max}, and R_A. The geometric mean and range will be presented for T_{max}.

Figures displaying the mean concentration over time, geometric mean with error bars, and per-subject concentration by time (with a separate line per subject) will be presented.

All plasma concentration data per-subject will be displayed in data listings.

Relevant Output

Table 14.2.8.1.1	Summary of Pharmacokinetic Concentrations by Visit and Timepoint (PK Population)
Table 14.2.8.1.2	Summary of Pharmacokinetic Parameters by Visit (PK Population)
Listing 16.2.5.2	Pharmacokinetic Concentrations
Listing 16.2.5.3	Pharmacokinetic Parameters

6. CHANGES TO PLANNED ANALYSES

Protocol Section 13.3.2.1 identifies the primary treatment effect parameter as the distribution of response classes. In this document, the primary treatment effect parameter is identified as the overall response rate, as this effect parameter was used during the sample size calculations described in Protocol Section 13.1. The distribution of response classes has been identified as a secondary efficacy parameter in this document.

Levels of MyD88 expression in tumor cells is identified in the protocol as an exploratory objective and anlysis. MyD88 is analyzed as a categorical factor (mutation present or absent), rather than continuous levels of expression.

Protocol Sections 2.7.1 and 10.8 state that PK data will be analyzed on a population basis. In this document it is described the analysis will not be a population PK analysis; it will be a standard non-compartmental PK analysis.

7. REFERENCES

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Owen RG, Kyle RA, Stone MJ, et al. Response Assessment in Waldenström's Macroglobulinemia: update from the VIth International Workshop. Br J Haematology 2012; 160:171-176.

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Young RM, **Staudt** LM. Targeting pathologic B cell receptor signaling in lymphoid malignancies. Nature Rev Drug Discovery. 2013; 12:229-243.

8. CLINICAL STUDY REPORT APPENDICES

8.1. List of Statistical Tables, Figures, and Listings to be Generated

8.2. Statistical Table and Figure Shells

The following statistical tables and figures will be produced.

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Table 14.0.1

Treatment Codes Applicable to Tables and Listings

Treatment Code	Treatment Description
0.6 mg/kg/wk	IMO-8400 at 0.6 mg/kg/wk
0.9 mg/kg/wk	IMO-8400 at 0.9 mg/kg/wk
1.2 mg/kg/wk	IMO-8400 at 1.2 mg/kg/wk
1.8 mg/kg/wk	IMO-8400 at 1.8 mg/kg/wk
2.4 mg/kg/wk	IMO-8400 at 2.4 mg/kg/wk
Total	Pooled IMO-8400 dosing groups

Note: Dosing is based on body weight at screening up to a maximum dose representing 125 kg equivalent.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

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Table 14.0.2

SI - US Unit Conversion

Lab Type	Laboratory Test	Unit Reported by Lab	Conversion Factor: Lab to SI Unit	SI Unit	Conversion Factor: SI to US Unit	US Unit

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

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Table 14.0.3

Laboratory Normal Ranges (US)

Lab Type	Lab Test	Lab Name	Range	Unit

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Table 14.1.1.1

Patient Enrollment and Disposition

Disposition	Sta-tistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Total Number of Patients Screened[1]	n	xx	xx	xx	xx	xx	xx
Total Number of Screen Failures[2]	n	xx	xx	xx	xx	xx	xx
Total Number of Patients Enrolled[3]	n	xx	xx	xx	xx	xx	xx
Study Populations							
Safety/ Intent-to-Treat [4]	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Per-Protocol[5]	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Pharmacokinetic[6]	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Discontinued Treatment	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Primary Reason for Treatment Discontinuation from EOT [7]							
DLT event	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Disease Progression	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Completion of 24 Weeks Treatment	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
AE, other than DLT	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Withdrawal of Consent	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Lost to Follow-Up	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Study Terminated by Sponsor	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Other	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)

Note: Unless otherwise noted, percentage is based on total number of patients enrolled (treated).
[1] Screened: Patients who signed consent and underwent screening procedure.
[2] Screen Failure: Screened patients deemed ineligible to enroll in the study due to failure to comply with incl/excl criteria.
[3] Enrolled: Patients who received at least one dose of study medication.
[4] All patients who received at least one dose of the study treatment.
[5] All patients who have one or more scheduled post-treatment tumor assessments, and no major protocol deviations.
[6] All patients with evaluable PK data based on protocol compliance, adequate number of samples and successful sample assays.
[7] EOT = End of Treatment. Percentage based on the number of patients who have discontinued treatment.
[8] Prematurely Discontinued Treatment: Patients who discontinued treatment prior to 24 weeks.
[9] EOS = End of Study. Percentage based on the number of patients who have prematurely discontinued treatment.
Reference Listing: 16.x.x.x

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Table 14.1.1.1

Patient Enrollment and Disposition

Disposition	Sta-tistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Prematurely Discontinued Treatment[10]	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Primary Reason for Premature Treatment Discontinuation from EOS [11]							
Disease Progression	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
AE, related to study treatment	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
AE, unrelated to study treatment	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Non-compliance	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Lost to Follow-Up	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Physician Decision	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Study Terminated by Sponsor	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)

Note: Unless otherwise noted, percentage is based on total number of patients enrolled (treated).
[1] Screened: Patients who signed consent and underwent screening procedure.
[2] Screen Failure: Screened patients deemed ineligible to enroll in the study due to failure to comply with incl/excl criteria.
[3] Enrolled: Patients who received at least one dose of study medication.
[4] All patients who received at least one dose of the study treatment.
[5] All patients who have one or more scheduled post-treatment tumor assessments, and no major protocol deviations.
[6] All patients with evaluable PK data based on protocol compliance, adequate number of samples and successful sample assays.
[7] Percentage based on the number of patients who have discontinued treatment.
[8] Prematurely Discontinued Treatment: Patients who discontinued treatment prior to 24 weeks.
[9] Percentage based on the number of patients who have prematurely discontinued treatment.
Reference Listing: 16.x.x.x

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Table 14.1.2.1

Demographic Characteristics (ITT/Safety Population)

Parameter	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Age (years) [1]	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Ethnicity							
Hispanic/Latino	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Not Hispanic/ Latino	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race							
American Indian or Alaska Native	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Asian	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Black	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Native Hawaiian or Other Pacific Islander	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
White							
Other	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Sex							
Male	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Female	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] Age calculated based on date of informed consent.

Reference Listing: 16.x.x.x

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Table 14.1.2.2

Baseline Characteristics (ITT/Safety Population)

Parameter	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Baseline Height (cm)	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Baseline Weight (kg)	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Baseline BMI (kg/m^2) [1]	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Baseline ECOG Performance Status							
0	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MyD88 mutation status							
Present	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Absent	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] Body Mass Index = Weight (kg)/(Height (m))^2.

Reference Listing: 16.x.x.x

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Table 14.1.3.1

Disease History (ITT/Safety Population)

Parameter	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Time Since WM Diagnosis (yrs) [1]	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min,Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Time Since First Treatment for WM (yrs) [2]	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min,Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
At least 1 Treatment Related AE in the past 3 months							
Yes	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
No	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subject has been hospitalized in the past year							
Yes	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
No	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Time since most recent hospitalization (months) [3]	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min,Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

[1] Time from WM diagnosis to date of first dose of study drug.
[2] Time from date of first treatment for WM to date of first dose of study drug.
[3] Time from most recent date of discharge to date of first dose of study drug.
Reference Listing: 16.x.x.x

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Table 14.1.4.1

Prior Treatments (ITT/Safety Population)

Parameter	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Received at least 1 Prior Therapy	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Agent/Treatment							
Rituximab	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Cyclophosphamide	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Doxorubicin	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Vincristine	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Prednisone	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Fludarabine	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Cladribine	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other							
Best Overall Response [1]							
Complete Response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Very Good Partial Response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Partial Response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Minor Response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Stable Disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Progressive Disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Not Evaluable	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Delayed Response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Prior Therapies	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min,Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Number of Days since Most Recent Prior Therapy [2]	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min,Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

[1] Percentages based on number that received at least 1 prior therapy.
[2] Time from end of prior therapy to date of first dose of IMO-8400.
Reference Listing: 16.x.x.x

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Programming note: Number of days since Most Recent Prior Therapy = (date of first dose – end date of most recent prior therapy) + 1

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Table 14.2.1.1.1

Objective Response Rate Primary Efficacy Analysis (ITT/Safety Population)

Parameter	Sta-tistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Objective Response Rate (CR/VGPR/PR/MR)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	90%CI	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx

Note: CR = Complete response. VGPR = Very good partial response. PR = Partial response. MR = Minor response.
Reference Listing: 16.x.x.x

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Repeat for:
Table 14.2.1.1.2 Objective Response Rate Primary Efficacy Analysis (PP Population)

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Table 14.2.1.2.1

Best Overall Response Secondary Efficacy Analysis (ITT/Safety Population)

Parameter	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Best Overall Response							
Complete response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Very good partial response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Partial response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Minor response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Stable disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Progressive disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Not evaluable	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Delayed response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Reference Listing: 16.x.x.x

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Programming note: Repeat on PP population only if the difference in number of patients between ITT and PP populations is >2.

Repeat for:
Table 14.2.1.2.2 Best Overall Response Secondary Efficacy Analysis (PP Population)

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Table 14.2.1.3.1

Duration of Objective Response Secondary Efficacy Analysis (PP Population)

Parameter	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Duration of Objective Response (DOR)	75th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
	25th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
Censored Observations	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Events	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: Subjects who have not progressed prior to the data cut-off for final efficacy analysis, who drop out prior to study end, or who pass away prior to documentation of disease progression will be censored at the date of the last valid disease assessment.
Reference Listing: 16.x.x.x

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Figure:
Figure 14.2.1.3.1 Duration of Objective Response Secondary Efficacy Analysis Kaplan-Meier Curve (PP Population)

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Table 14.2.1.4.1

Time to Progression Secondary Efficacy Analysis (ITT/Safety Population)

Parameter	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Time to Progression (TTP)	75th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
	25th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
Censored Observations	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Events	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: Subjects who have not progressed prior to the data cut-off for final efficacy analysis, or who drop out prior to study end, will be censored at the day they were last known to be progression-free date of the last valid disease assessment.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Repeat on PP population only if the difference in number of patients between ITT and PP populations is >2.

Figure:
  Figure 14.2.1.4.1 Time to Progression Secondary Efficacy Analysis Kaplan-Meier Curve (ITT/Safety Population)

Repeat for:
  Table 14.2.1.4.2 Time to Progression Secondary Efficacy Analysis (PP Population)
  Figure 14.2.1.4.2 Time to Progression Secondary Efficacy Analysis Kaplan-Meier Curve (PP Population)

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Table 14.2.1.5.1

Progression-Free Survival Secondary Efficacy Analysis (PP Population)

Parameter	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Progression-Free Survival (PFS)	75th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
	25th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
Censored Observations	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Events	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: Subjects who have not progressed prior to the data cut-off for final efficacy analysis, or who drop out prior to study end, will be censored at the date of the last valid disease assessment.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Figure:
Figure 14.2.1.5.1 Progression-Free Survival Secondary Efficacy Analysis Kaplan-Meier Curve (PP Population)

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Table 14.2.1.6.1

Time to Best Observed Response Secondary Efficacy Analysis (PP Population)

Parameter	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Time to Best Observed Response	75th Percentile (90% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	Median (90% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	25th Percentile (90% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
Censored Observations	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Events	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: Patients who do not have a response recorded will be censored at date of first treatment dose.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Figure:
Figure 14.2.1.6.1 Time to Best Observed Response Secondary Efficacy Analysis Kaplan-Meier Curve (PP Population)

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Table 14.2.2.1.1

Objective Response Rate Primary Efficacy Analysis by MyD88 Mutation Status (ITT/Safety Population)

Parameter	Mutation Status	Sta-tistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Objective Response Rate (CR/VGPR/PR/MR)	Present	n(%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		90% CI	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx
	Absent	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		90% CI	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx

Note: CR = Complete response. VGPR = Very good partial response. PR = Partial response. MR = Minor response.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Repeat on PP population only if the difference in number of patients between ITT and PP populations is >2.

Repeat for:
Table 14.2.2.1.2 Objective Response Rate Primary Efficacy Analysis by MyD88 Mutation Status (PP Population)

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Table 14.2.2.2.1

Best Overall Response Secondary Efficacy Analysis by MyD88 Mutation Status (PP Population)

Mutation Status	Best Overall Response	Sta-tistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Present	Complete response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Very good partial response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Partial response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Minor response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Stable disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Progressive disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Not evaluable	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Delayed response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Absent	Complete response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Very good partial response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Partial response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Minor response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Stable disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Progressive disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Not evaluable	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Delayed response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Reference Listing: 16.x.x.x

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Table 14.2.2.4.1

Time to Progression Secondary Efficacy Analysis by MyD88 Mutation Status (PP Population)

Mutation Status	Parameter	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Present	TTP	75th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
		25th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
	Censored Observations	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Event Rate	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Absent	TTP	75th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
		25th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		(90% CI)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
	Censored Observations	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Event Rate	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: TTP = Time to Progression. Subjects who have not progressed prior to the data cut-off for final efficacy analysis, or who drop out prior to study end, are censored at the day they were last known to be progression-free date of the last valid disease assessment.
Reference Listing: 16.x.x.x

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Figure:
Figure 14.2.2.4.1 Time to Progression Secondary Efficacy Analysis by MyD88 Mutation Status Kaplan-Meier Curve (PP Population)

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Table 14.2.3.1.1

Percent Change from Baseline in Quantitative Serum Levels of Total IgM (ITT/Safety Population)

		0.6 mg/kg/wk (N=xx)		0.9 mg/kg/wk (N=xx)		1.2 mg/kg/wk (N=xx)	
Visit	Statistic	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
Baseline	n	xx	--	xx	--	xx	--
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx.x		xx.x		xx.x	
	Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
C1W9	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Etc.							

Note: Baseline = the most recent laboratory assessments before the first dose of study medication.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Move onto 2 pages as needed; include all dose groups and total (0.6, 0.9, 1.2, 1.8, 2.4, and total), see following page. For the Box plot figures, include standard deviation as error bars.
Programming note: Repeat on PP population only if the difference in number of patients between ITT and PP populations is >2.

Figure:
  Figure 14.2.3.1.1 Percent Change from Baseline in Quantitative Serum Levels of Total IgM Box Plot (ITT/Safety Population)

Repeat for:
  Table 14.2.3.1.2 Percent Change from Baseline in Quantitative Serum Levels of Total IgM (PP Population)
  Figure 14.2.3.1.2 Percent Change from Baseline in Quantitative Serum Levels of Total IgM Box Plot (PP Population)

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Table 14.2.3.1.1

Percent Change from Baseline in Quantitative Serum Levels of Total IgM (ITT/Safety Population)

		1.8 mg/kg/wk (N=xx)		2.4 mg/kg/wk (N=xx)		Total (N=xx)	
Visit	Statistic	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
Baseline	n	xx	--	xx	--	xx	--
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx.x		xx.x		xx.x	
	Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
C1W9	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Etc.							

Note: Baseline = the most recent laboratory assessments before the first dose of study medication.
Reference Listing: 16.x.x.x

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Table 14.2.3.2.1

Change from Baseline in Quantitative Serum Levels of Total IgM (ITT/Safety Population)

		0.6 mg/kg/wk (N=xx)		0.9 mg/kg/wk (N=xx)		1.2 mg/kg/wk (N=xx)	
Visit	Statistic	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
Baseline	n	xx	--	xx	--	xx	--
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx.x		xx.x		xx.x	
	Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
C1W9	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Etc.							

Note: Baseline = the most recent laboratory assessments before the first dose of study medication.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Move onto 2 pages as needed; include all dose groups and total (0.6, 0.9, 1.2, 1.8, 2.4, and total), see following page. For the Box plot figures, include standard deviation as error bars.
Programming note: Repeat on PP population only if the difference in number of patients between ITT and PP populations is >2.

Figure:
  Figure 14.2.3.2.1 Change from Baseline in Quantitative Serum Levels of Total IgM Box Plot (ITT/Safety Population)

Repeat for:
  Table 14.2.3.2.2 Change from Baseline in Quantitative Serum Levels of Total IgM (PP Population)
  Figure 14.2.3.2.2 Change from Baseline in Quantitative Serum Levels of Total IgM Box Plot (PP Population)

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Table 14.2.3.2.1

Change from Baseline in Quantitative Serum Levels of Total IgM (ITT/Safety Population)

		1.8 mg/kg/wk (N=xx)		2.4 mg/kg/wk (N=xx)		Total (N=xx)	
Visit	Statistic	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
Baseline	n	xx	--	xx	--	xx	--
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx.x		xx.x		xx.x	
	Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
C1W9	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Etc.							

Note: Baseline = the most recent laboratory assessments before the first dose of study medication.
Reference Listing: 16.x.x.x

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Table 14.2.4.1.1

Percent Change from Baseline in Quantitative Serum Levels of Total IgM by MyD88 Mutation Status (PP Population)

			0.6 mg/kg/wk (N=xx)		0.9 mg/kg/wk (N=xx)		1.2 mg/kg/wk (N=xx)	
Visit	Mutation Status	Statistic	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
Baseline	Present	n	xx	--	xx	--	xx	--
		Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
		Median	xx.x		xx.x		xx.x	
		Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
	Absent	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
C1W9	Present	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	Absent	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x

Etc.

Note: Baseline = the most recent laboratory assessments before the first dose of study medication.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Move onto 2 pages as needed; include all dose groups and total (0.6, 0.9, 1.2, 1.8, 2.4, and total), see following page. For the Box plot figures, include standard deviation as error bars.

Figure:
Figure 14.2.4.1.1 Percent Change from Baseline in Quantitative Serum Levels of Total IgM by MyD88 Mutation Status Box Plot (PP Population)

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Table 14.2.4.1.1

Percent Change from Baseline in Quantitative Serum Levels of Total IgM by MyD88 Mutation Status (PP Population)

			1.8 mg/kg/wk (N=xx)		2.4 mg/kg/wk (N=xx)		Total (N=xx)	
Visit	Mutation Status	Statistic	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
Baseline	Present	n	xx	--	xx	--	xx	--
		Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
		Median	xx.x		xx.x		xx.x	
		Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
	Absent	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
C1W9	Present	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	Absent	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Etc.								

Note: Baseline = the most recent laboratory assessments before the first dose of study medication.
Reference Listing: 16.x.x.x

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Table 14.2.4.2.1

Change from Baseline in Quantitative Serum Levels of Total IgM by MyD88 Mutation Status (PP Population)

			0.6 mg/kg/wk (N=xx)		0.9 mg/kg/wk (N=xx)		1.2 mg/kg/wk (N=xx)	
Visit	Mutation Status	Statistic	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
Baseline	Present	n	xx	--	xx	--	xx	--
		Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
		Median	xx.x		xx.x		xx.x	
		Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
	Absent	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
C1W9	Present	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	Absent	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x

Etc.

Note: Baseline = the most recent laboratory assessments before the first dose of study medication.
Reference Listing: 16.x.x.x

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Programming note: Move onto 2 pages as needed; include all dose groups and total (0.6, 0.9, 1.2, 1.8, 2.4, and total), see following page. For the Box plot figures, include standard deviation as error bars.

Figure:
Figure 14.2.4.2.1 Change from Baseline in Quantitative Serum Levels of Total IgM by MyD88 Mutation Status Box Plot (PP Population)

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Table 14.2.4.2.1

Change from Baseline in Quantitative Serum Levels of Total IgM by MyD88 Mutation Status (PP Population)

			1.8 mg/kg/wk (N=xx)		2.4 mg/kg/wk (N=xx)		Total (N=xx)	
Visit	Mutation Status	Statistic	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
Baseline	Present	n	xx	--	xx	--	xx	--
		Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
		Median	xx.x		xx.x		xx.x	
		Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
	Absent	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
C1W9	Present	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	Absent	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Etc.								

Note: Baseline = the most recent laboratory assessments before the first dose of study medication.
Reference Listing: 16.x.x.x

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Table 14.2.5.1.1

Change in Quantitative Serum Levels of Total IgM – Repeated Measures Analysis (ITT/Safety Population)

Parameter	Statistic	Global Test [1]	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)
Visit	p-value	0.xxxx					
Treatment	p-value	0.xxxx					
Treatment*Visit	p-value	0.xxxx					
Baseline Value	p-value	0.xxxx					
Dose group vs. 0.6 mg/kg/wk	Estimate [2]			x.xx	x.xx	x.xx	x.xx
	90% CI	NA	NA	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
	P-value			0.xxxx	0.xxxx	0.xxxx	0.xxxx
Dose group vs. 0.9 mg/kg/wk	Estimate		x.xx		x.xx	x.xx	x.xx
	90% CI	NA	x.x, x.x	NA	x.x, x.x	x.x, x.x	x.x, x.x
	P-value		0.xxxx		0.xxxx	0.xxxx	0.xxxx
Dose group vs. 1.2 mg/kg/wk	Estimate		x.xx	x.xx		x.xx	x.xx
	90% CI	NA	x.x, x.x	x.x, x.x	NA	x.x, x.x	x.x, x.x
	P-value		0.xxxx	0.xxxx		0.xxxx	0.xxxx
Dose group vs. 1.8 mg/kg/wk	Estimate		x.xx	x.xx	x.xx		x.xx
	90% CI	NA	x.x, x.x	x.x, x.x	x.x, x.x	NA	x.x, x.x
	P-value		0.xxxx	0.xxxx	0.xxxx		0.xxxx
Dose group vs. 2.4 mg/kg/wk	Estimate		x.xx	x.xx	x.xx	x.xx	
	90% CI	NA	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	NA
	P-value		0.xxxx	0.xxxx	0.xxxx	0.xxxx	

Note: Model based on a repeated-measures mixed-model (PROC MIXED in SAS) with response variable change from baseline, fixed factors for treatment, visit and treatment by visit interaction, and baseline value and MyD88 mutation status as covariates.
[1] Type 3 tests (Global F test)
[2] Footnote where estimate/ p-value is coming from
NA = Not applicable.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Compare the individual dose groups only if the global test is statistically significant.
Programming note: Repeat on PP population only if the difference in number of patients between ITT and PP populations is >2.

Repeat for:
Table 14.2.5.1.2 Change in Quantitative Serum Levels of Total IgM – Repeated Measures Analysis (PP Population)

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Table 14.2.5.2.1

Change in Quantitative Serum Levels of Total IgM – Repeated Measures Analysis Least Square Means by Visit (ITT/Safety Population)

Visit	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)
Day 1	LS Means	x.x	x.x	x.x	x.x	x.x
	SE	x.xx	x.xx	x.xx	x.xx	x.xx
	90% CI	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
Day 15	LS Means	x.x	x.x	x.x	x.x	x.x
	SE	x.xx	x.xx	x.xx	x.xx	x.xx
	90% CI	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
Etc.	LS Means	x.x	x.x	x.x	x.x	x.x
	SE	x.xx	x.xx	x.xx	x.xx	x.xx
	90% CI	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x

Note: LS = Least-squares. SE = Standard Error. CI = Confidence Interval. Model based on a repeated-measures mixed-model (PROC MIXED in SAS) with response variable change from baseline, fixed factors for treatment, visit and treatment by visit interaction, and baseline value and MyD88 mutation status as covariates.
Reference Listing: 16.x.x.x

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Programming note: Present the least square means estimate figures with standard deviation as error bars.
Programming note: Repeat on PP population only if the difference in number of patients between ITT and PP populations is >2.

Figure:
Figure 14.2.5.2.1 Change in Quantitative Serum Levels of Total IgM - Repeated Measures Analysis: Least Square Means over Time(ITT/Safety Population)

Repeat for:
Table 14.2.5.2.2 Change in Quantitative Serum Levels of Total IgM – Repeated Measures Analysis (PP Population)
Figure 14.2.5.2.2 Change in Quantitative Serum Levels of Total IgM - Repeated Measures Analysis: Least Square Means over Time (PP Population)

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Table 14.2.8.1.1

Summary of Pharmacokinetic Concentrations by Visit and Timepoint (PK Population)

Visit	Timepoint	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Day 1	Pre-dose	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	1 hour post-dose	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	2 hours post-dose	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	4 hours post-dose	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x

Reference Listing: 16.x.x.x

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Table 14.2.8.1.2

Summary of Pharmacokinetic Parameters by Visit (PK Population)

Parameter	Visit	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Cmax (ng/mL)	Day 1	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
		CV%	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Day 15	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
		CV%	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Etc.							
AUC0-last	Day 1	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
		CV%	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Etc.							
Tmax	Day 1	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	Etc.							
RA	Day 1	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
		CV%	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Etc.							

Reference Listing: 16.x.x.x

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Programming note: Include all visits and PK parameters.

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Table 14.3.1.1

Summary of Adverse Events (ITT/Safety Population)

Parameter	Sta-tistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
At Least 1 AE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least 1 Injection Site Reaction	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least 1 TEAE [1]	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least 1 Related TEAE [1]	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least 1 Grade >=3 TEAE [1]	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least 1 SAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least 1 DLT	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] Other than injection site reactions.
Note: At least 1 = Any. AE = Adverse Event. TEAE = Treatment-Emergent Adverse Event. SAE = Serious Adverse Event. DLT = Dose Limiting Toxicity.
Reference Listing: 16.x.x.x

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Table 14.3.1.2

Incidence of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term (ITT/Safety Population)

MedDRA SOC / Preferred Term	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
At Least 1 TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.							

Note: TEAE = Treatment-Emergent Adverse Event.
Reference Listing: 16.x.x.x

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Table 14.3.1.3

Incidence of Treatment-Emergent Adverse Events by Relationship to Study Drug and by MedDRA System Organ Class and Preferred Term
(ITT/Safety Population)

		0.6 mg/kg/wk (N=xx)		0.9 mg/kg/wk (N=xx)		1.2 mg/kg/wk (N=xx)	
MedDRA SOC / Preferred Term	Sta-tistic	Drug-Related	Not Drug-Related	Drug-Related	Not Drug-Related	Drug-Related	Not Drug-Related
At Least 1 TEAE	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
SOC 1	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Preferred Term 1	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Preferred Term 2	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Etc.	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Etc.							

Note: TEAE = Treatment-Emergent Adverse Event. Drug related adverse events are those which are identified by the investigator as probably or possibly related to the study drug and not related adverse events are those which are unlikely and not related to the study drug. The most related occurrence is counted if the patient experienced multiple occurrences of the same adverse event.
Reference Listing: 16.x.x.x

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Programming note: Move onto 2 pages as needed; include all dose groups and total (0.6, 0.9, 1.2, 1.8, 2.4, and total), see following page.

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Table 14.3.1.3

Incidence of Treatment-Emergent Adverse Events by Relationship to Study Drug and by MedDRA System Organ Class and Preferred Term
(ITT/Safety Population)

		1.8 mg/kg/wk (N=xx)		2.4 mg/kg/wk (N=xx)		Total (N=xx)	
MedDRA SOC / Preferred Term	Sta-tistic	Drug-Related	Not Drug-Related	Drug-Related	Not Drug-Related	Drug-Related	Not Drug-Related
At Least 1 TEAE	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
SOC 1	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Preferred Term 1	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Preferred Term 2	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Etc.	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Etc.							

Note: TEAE = Treatment-Emergent Adverse Event. Drug related adverse events are those which are identified by the investigator as probably or possibly related to the study drug and not related adverse events are those which are unlikely and not related to the study drug. The most related occurrence is counted if the patient experienced multiple occurrences of the same adverse event.
Reference Listing: 16.x.x.x

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Table 14.3.1.4

Incidence of Non-Serious Adverse Events, by MedDRA System Organ Class and Preferred Term (Safety Population)

MedDRA SOC / Preferred Term	Statistic	0.6 mpk (N=xx)	0.9 mpk (N=xx)	1.2 mpk (N=xx)	1.8 mpk (N=xx)	2.4 mpk (N=xx)	Total (N=xx)
SOC 1	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 2	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	N (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.							

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Table 14.3.1.5

Incidence of Treatment-Emergent Adverse Events by Intensity and by MedDRA System Organ Class and Preferred Term
(ITT/Safety Population)

		0.6 mg/kg/wk (N=xx)			0.9 mg/kg/wk (N=xx)			1.2 mg/kg/wk (N=xx)		
MedDRA SOC / Preferred Term	Sta-tistic	Grade 1 or 2	Grade >= 3	Total	Grade 1 or 2	Grade >= 3	Total	Grade 1 or 2	Grade >= 3	Total
At Least 1 TEAE	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
SOC 1	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Preferred Term 1	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Preferred Term 2	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Etc.	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Etc.										

Note: TEAE = Treatment-Emergent Adverse Event. The highest intensity occurrence is counted if the patient experienced multiple occurrences of the same adverse event.
Reference Listing: 16.x.x.x

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Programming note: Move onto 2 pages as needed; include all dose groups and total (0.6, 0.9, 1.2, 1.8, 2.4, and total), see following page.

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Table 14.3.1.5

Incidence of Treatment-Emergent Adverse Events by Intensity and by MedDRA System Organ Class and Preferred Term
(ITT/Safety Population)

		1.8 mg/kg/wk (N=xx)			2.4 mg/kg/wk (N=xx)			Total (N=xx)		
MedDRA SOC / Preferred Term	Sta-tistic	Grade 1 or 2	Grade >= 3	Total	Grade 1 or 2	Grade >= 3	Total	Grade 1 or 2	Grade >= 3	Total
At Least 1 TEAE	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
SOC 1	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Preferred Term 1	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Preferred Term 2	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Etc.	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Etc.										

Note: TEAE = Treatment-Emergent Adverse Event. The highest intensity occurrence is counted if the patient experienced multiple occurrences of the same adverse event.
Reference Listing: 16.x.x.x

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Table 14.3.1.6

Incidence of Dose-Limiting Toxicity Adverse Events by MedDRA System Organ Class and Preferred Term (ITT/Safety Population)

MedDRA SOC / Preferred Term	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
At Least 1 DLT	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: DLT = Dose-Limiting Toxicity.
Reference Listing: 16.x.x.x

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Table 14.3.1.7

Incidence of Local Injection Site Reactions Worst Grade Post Baseline (ITT/Safety Population)

Symptom / Toxicity Grade	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Pain							
Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Tenderness							
Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
<Repeat above format for Pruritus and Induration>							
Blister							
Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Blister (mm)	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	25th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	75th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	90th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
<Repeat above format (2 rows each) for Ulceration and Necrosis>							

Note: In the case of multiple grades, only the worst grade post baseline is counted for each subject and symptom regardless of the site of injection.
Reference Listing: 16.x.x.x

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Table 14.3.1.8

Incidence of Local Injection Site Reactions Worst Grade by Visit (ITT/Safety Population)

Visit	Symptom / Toxicity Grade	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Day 1	Pain							
	Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Tenderness							
	Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.							
Day 3	Pain							
	Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Tenderness							
	Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.							
Etc.								

Note: In the case of multiple grades, only the worst grade at each visit is counted for each subject and symptom regardless of the site of injection.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Include all symptoms and all visits.

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Table 14.3.2.1

Listing of Deaths

Dose Group	Patient Number	SOC	Preferred Term	Onset Date/Time	Onset Rel Day [1]	End Date/Time	End Rel Day [1]	Severity [2]	Serious	Relationship [3]	Action Taken with IMO-8400	Action Taken for AE	Sequelae at Resolution
									Yes				Yes
									No				No

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] 1 = Grade 1: Mild. 2 = Grade 2: Moderate. 3 = Grade 3: Marked. 4 = Grade 4: Extreme. 5 = Grade 5: Death.
[3] Relationship to Study Drug: Prob Rel = Probably Related, Poss Rel = Possibly Related, Unlike Rel = Unlikely Related, Not Rel = Not related.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If sequelae at resolution, concatenate specifics (Yes: Specify sequelae).

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Table 14.3.2.2

Listing of Serious Adverse Events

				Onset		End						
Dose Group	Patient Number	SOC	Preferred Term	Date/ Time	Rel Day [1]	Date/Time	Rel Day [1]	Severity [2]	Relationship [3]	Action Taken with IMO-8400	Action Taken for AE	Sequelae at Resolution
												Yes
												No

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] 1 = Grade 1: Mild. 2 = Grade 2: Moderate. 3 = Grade 3: Marked. 4 = Grade 4: Extreme. 5 = Grade 5: Death.
[3] Relationship to Study Drug: Prob Rel = Probably Related, Poss Rel = Possibly Related, Unlike Rel = Unlikely Related, Not Rel = Not related.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If sequelae at resolution, concatenate specifics (Yes: Specify sequelae).

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Table 14.3.2.3

Listing of Treatment Discontinuations Due to Adverse Events

Dose Group	Patient Number	SOC	Preferred Term	Onset Date/ Time	Onset Rel Day [1]	End Date/ Time	End Rel Day [1]	Sever- ity [2]	Serious	Rela- tionship [3]	Action Taken with IMO-8400	Action Taken for AE	Sequelae at Resolution
									Yes				Yes
									No				No

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] 1 = Grade 1: Mild. 2 = Grade 2: Moderate. 3 = Grade 3: Marked. 4 = Grade 4: Extreme. 5 = Grade 5: Death.
[3] Relationship to Study Drug: Prob Rel = Probably Related, Poss Rel = Possibly Related, Unlike Rel = Unlikely Related, Not Rel = Not related.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If sequelae at resolution, concatenate specifics (Yes: Specify sequelae).

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Table 14.3.4.1

Listing of Clinically Significant Abnormal Laboratory Values (ITT/ Safety Population)

Dose Group	Patient Number	Date of Collection	Rel Day [1]	Lab Test	Results	Unit	Normal Range		CTCAE Grade
							Lower Limit	Upper Limit	

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
Note: LP - Low Panic, L - Low Normal, H - High Normal, HP - High Panic, AB – Abnormal.
Reference Listing: 16.x.x.x

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Table 14.3.5.1

Study Drug Exposure (ITT/Safety Population)

Parameter	Statistics	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Cumulative dose [1]	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Cycles Received							
Received 1 cycle	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Received 2 cycles	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Received 3 cycles	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Received 4 cycles	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number missed doses	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Reason dose missed							
DLT	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
AE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit missed	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] Cumulative dose is the dose injected multiplied times the number of injections.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Repeat for:
Table 14.3.5.2 Study Drug Exposure (PP Population)

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Table 14.3.5.3

Summary and Change from Baseline for Hematology Parameters by Time Point and Dose Group (ITT/Safety Population)

			0.6 mg/kg/wk (N=xx)		0.9 mg/kg/wk (N=xx)		1.2 mg/kg/wk (N=xx)	
Laboratory Parameter	Visit	Statistic	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
Lab Test 1 (unit)	Baseline	n	xx	--	xx	--	xx	--
		Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
		Median	xx.x		xx.x		xx.x	
		Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
	C1W2	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	Etc.							
Lab Test 2 (unit)	Baseline	n	xx	--	xx	--	xx	--
		Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
		Median	xx.x		xx.x		xx.x	
		Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
	C1W2	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	Etc.							

Note: Baseline = the most recent laboratory assessments before the first dose of study medication.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note: Repeat analyses for all laboratory parameters. Move onto 2 pages as needed; include all dose groups and total (0.6, 0.9, 1.2, 1.8, 2.4, and total), see following page. For the Box plot figures, include standard deviation as error bars.

Figure:
Figure 14.3.5.3 Summary and Change from Baseline for Hematology Parameters by Time Point and Dose Group - Box Plot (ITT/Safety Population)

Repeat for:
Table 14.3.5.4 Summary and Change from Baseline for Chemistry Parameters by Time Point and Dose Group (ITT/Safety Population)
Figure 14.3.5.4 Summary and Change from Baseline for Chemistry Parameters by Time Point and Dose Group - Box Plot (ITT/Safety Population)
Table 14.3.5.5 Summary and Change from Baseline for Coagulation Parameters by Time Point and Dose Group (ITT/Safety Population)
Figure 14.3.5.5 Summary and Change from Baseline for Coagulation Parameters by Time Point and Dose Group - Box Plot (ITT/Safety Population)

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Table 14.3.5.3

Summary and Change from Baseline for Hematology Parameters by Time Point and Dose Group (ITT/Safety Population)

			1.8 mg/kg/wk (N=xx)		2.4 mg/kg/wk (N=xx)		Total (N=xx)	
Laboratory Parameter	Visit	Statistic	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
Lab Test 1 (unit)	Baseline	n	xx	--	xx	--	xx	--
		Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
		Median	xx.x		xx.x		xx.x	
		Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
	C1W2	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	Etc.							
Lab Test 2 (unit)	Baseline	n	xx	--	xx	--	xx	--
		Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
		Median	xx.x		xx.x		xx.x	
		Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
	C1W2	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	Etc.							
Etc.								

Note: Baseline = the most recent laboratory assessments before the first dose of study medication.
Reference Listing: 16.x.x.x

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Table 14.3.5.6A

Shifts from Baseline to Worst CTC Grade Post-Baseline in Hematology Parameters by Dose Group (ITT/Safety Population)

Laboratory Parameter	Dose Group	Baseline Results	Statistic	Worst CTC Grade Post-Baseline Results: WNL	Grade 1	Grade 2	Grade 3	Grade 4	Missing
Lab Test 1 (unit)	0.6 mg/kg/wk	WNL	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Missing	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0.9 mg/kg/wk	WNL	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Missing	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.								
Lab Test 2 (unit)	0.6 mg/kg/wk	WNL	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Missing	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.								
Etc.									

Note: Baseline = the most recent laboratory assessments before the first dose of study medication. WNL = Within Normal Limit.
Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note: Repeat analyses for all laboratory parameters and all visits. Include all dose groups and total (0.6, 0.9, 1.2, 1.8, 2.4, and total).

Repeat for:
Table 14.3.5.6B Shifts from Baseline to Worst CTC Grade Post-Baseline in Chemistry Parameters by Dose Group (ITT/Safety Population)
Table 14.3.5.6C Shifts from Baseline to Worst CTC Grade Post-Baseline in Coagulation Parameters by Dose Group (ITT/Safety Population)

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Table 14.3.5.7

Summary and Change from Baseline for Vital Signs by Time Point and Dose Group (ITT/Safety Population)

			0.6 mg/kg/wk (N=xx)		0.9 mg/kg/wk (N=xx)		1.2 (N=xx)	
Parameter	Visit	Statistic	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
Temperature (°C)	Baseline	n	xx	--	xx	--	xx	--
		Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
		Median	xx.x		xx.x		xx.x	
		Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
	C1W2	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	Etc.							
Etc.								

Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note: Repeat analyses for all vital sign parameters. Move onto 2 pages as needed; include all dose groups and total (0.6, 0.9, 1.2, 1.8, 2.4, and total). For the Box plot figures, include standard deviation as error bars.

Figure:
Figure 14.3.5.7 - Summary and Change from Baseline for Vital Signs by Time Point and Dose Group - Box Plot (ITT/Safety Population)

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Table 14.3.5.7

Summary and Change from Baseline for Vital Signs by Time Point and Dose Group (ITT/Safety Population)

			1.8 mg/kg/wk (N=xx)		2.4 mg/kg/wk (N=xx)		Total (N=xx)	
Parameter	Visit	Statistic	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
Temperature (°C)	Baseline	n	xx	--	xx	--	xx	--
		Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
		Median	xx.x		xx.x		xx.x	
		Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
	C1W2	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	Etc.							
Etc.								

Reference Listing: 16.x.x.x

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Table 14.3.5.8

Summary and Change from Baseline for Electrocardiogram Results by Time Point and Dose Group (ITT/Safety Population)

			0.6 mg/kg/wk (N=xx)		0.9 mg/kg/wk (N=xx)		1.2 (N=xx)	
ECG Parameter	Visit	Statistic	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
HR (bpm)	Baseline	n	xx	--	xx	--	xx	--
		Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
		Median	xx.x		xx.x		xx.x	
		Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
	C1W2	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	Etc.							
Etc.								

Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note: Repeat analyses for all vital sign parameters. Move onto 2 pages as needed; include all dose groups and total (0.6, 0.9, 1.2, 1.8, 2.4, and total).

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Table 14.3.5.8

Summary and Change from Baseline for Electrocardiogram Results by Time Point and Dose Group (ITT/Safety Population)

			1.8 mg/kg/wk (N=xx)		2.4 mg/kg/wk (N=xx)		Total (N=xx)	
ECG Parameter	Visit	Statistic	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
HR (bpm)	Baseline	n	xx	--	xx	--	xx	--
		Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
		Median	xx.x		xx.x		xx.x	
		Min,Max	xx.x,xx.x		xx.x,xx.x		xx.x,xx.x	
	C1W2	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	Etc.							
Etc.								

Reference Listing: 16.x.x.x

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note: Repeat analyses for all vital sign parameters. Move onto 2 pages as needed; include all dose groups and total (0.6, 0.9, 1.2, 1.8, 2.4, and total).

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Table 14.3.5.9

Listing of Abnormal Electrocardiogram Assessments (ITT/Safety Population)

Dose Group	Patient Number	Date/Time of Assessment	Rel Day [1]	Ventricular Rate (bpm)	RR Interval (msec)	PR Interval (msec)	QRS Interval (msec)	QT Interval (msec)	QTc Interval (msec)	QTc Interval Method	ECG Result

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
Reference Listing: 16.x.x.x

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Programming note: Include where ECG Result = “Abnormal, Not clinically significant” or “Abnormal, clinically significant”.

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Table 14.3.5.10

Concomitant Medications (ITT/Safety Population)

ATC Classification	Statistic	0.6 mg/kg/wk (N=xx)	0.9 mg/kg/wk (N=xx)	1.2 mg/kg/wk (N=xx)	1.8 mg/kg/wk (N=xx)	2.4 mg/kg/wk (N=xx)	Total (N=xx)
Any Concomitant Medication	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CM CLASS 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CM Code 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CM Code 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CM CLASS 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CM Code 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CM Code 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.							

Reference Listing: 16.x.x.x

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Programming Note: Repeat analyses for all CM classes and CM codes.

8.3. Data Listing Shells

The following data listings will be produced.

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Listing 16.0.1

System Organ Class Abbreviations

SOC	Abbreviations
Blood and lymphatic system disorders	BLOOD
Cardiac disorders	CARD
Congenital, familial and genetic disorders	CONGN
Ear and labyrinth disorders	EAR
Endocrine disorders	ENDO
Eye disorders	EYE
Gastrointestinal disorders	GASTR
General disorders and administration site conditions	GENRL
Hepatobiliary disorders	HEPAT
Immune system disorders	IMMUN
Infections and infestations	INFCT
Injury, poisoning and procedural complications	INJUR
Investigations	INVST
Metabolism and nutrition disorders	METAB
Musculoskeletal and connective tissue disorders	MUSCL
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	NEOPL
Nervous system disorders	NERV
Pregnancy, puerperium and perinatal conditions	PREG
Psychiatric disorders	PSYCH
Renal and urinary disorders	RENAL
Reproductive system and breast disorders	REPRO
Respiratory, thoracic and mediastinal disorders	RESP
Skin and subcutaneous tissue disorders	SKIN
Social circumstances	SOCL
Surgical and medical procedures	SURG
Vascular disorders	VASC

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: Verify the list of abbreviations includes all SOCs.

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Listing 16.2.1.1

Patients Discontinuing Treatment Prematurely

Dose Group	Patient Number	Number of Cycles Received	Date of Last Dose	Rel Day [1]	Reason Discontinued

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: Reason discontinued taken from “Please indicate the primary reason patient did not complete all weeks” question.

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Listing 16.2.1.2

End of Treatment (EOT) Visit Status

Dose Group	Patient Number	Date of Treatment Termination	Rel Day [1]	Primary Reason for Termination of Treatment	Specifics	Comments	Date of EOT visit	Rel Day [1]
				DLT event				
				Disease Progression				
				Completion of 24 weeks treatment				
				AE				
				Withdrawal of Consent				
				Lost to Follow-Up				
				Study Termination by Sponsor				
				Other				

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: Primary reason for termination of treatment taken from the EOT page. Include additional specification under "Specifics". Include "Please specify DLT event", "Please specify disease progression", "Please specify other adverse event", "Please explain all attempts to contact the subject", and "Please specify other".

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Listing 16.2.1.3

End of Study (EOS) Visit Status

Dose Group	Patient Number	Date of Visit	Rel Day [1]	Reason Visit Not Completed	Date of Death	Rel Day [1]	Cause of Death	Date Last Seen	Rel Day [1]	Completed 24 Weeks of Study Treatment	Primary Reason Patient did not Complete 24 Weeks	Comments
				Death						Yes	Disease Progression	
				Lost to Follow-up						No	AE related to study treatment	
				Withdrawal of Consent							AE not related to study treatment	
											Pregnancy	
											Lost to Follow-up	
											Withdrawal of Consent	
											Physician Decision	
											Study terminated by Sponsor	

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.2.1

Inclusion Criteria

Criterion Number	Inclusion Criteria
IN-1	Be at least 18 years of age.
IN-2	Have signed the current approved informed consent form.
IN-3	For women of childbearing potential and men, agree to use effective contraceptive methods from screening, through the study, and for at least 4 weeks after the last dose of study drug.
IN-4	For women of childbearing potential, have a negative serum pregnancy test at screening.
IN-5	Be willing and able to comply with this protocol.

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Listing 16.2.2.2

Exclusion Criteria

Criterion Number	Exclusion Criteria
EX-1	Has known hypersensitivity to any oligodeoxynucleotide.
EX-2	Is nursing.
EX-3	Has body weight <50 kg.
EX-4	Has BMI >34.9 kg/m^2.
EX-5	Has an indeterminate or positive test for antibody to human immunodeficiency virus (HIV-1 or -2) or hepatitis C virus (HCV).
EX-6	Has a positive test for hepatitis B surface antigen (HBsAg).
EX-7	Has, at screening, safety laboratory tests meeting one or more of the following criteria: – Hemoglobin <7.5 g/dL – Serum creatinine >2.5x ULN
EX-8	Has, at screening, any other safety laboratory tests that are Grade 2 or higher based on NCI CTCAE criteria.
EX-9	Is, at the initiation of study drug, receiving chronic systemic corticosteroid therapy >20 mg of prednisone daily (or equivalent); steroids administered topically or by inhalation are permitted.
EX-10	Has, at the initiation of study drug, received cytotoxic chemotherapy within the past three (3) weeks or rituximab within the past two (2) months; for other anti-cancer therapies (approved or investigational) the interval will be determined in consultation with the Medical Monitor.
EX-11	Has, at the initiation of study drug, an active infection requiring systemic antibiotics.
EX-12	Has had within the 4 weeks prior to initiation of study drug, or is expected to have during the study period, surgery requiring general anesthesia.
EX-13	Has active autoimmune cytopenia (anemia, thrombocytopenia, leukopenia) requiring concomitant therapy.
EX-14	Has life expectancy of less than 3 months.
EX-15	Has performance status of Grade 3 or 4 (Eastern Cooperative Oncology Group [ECOG] criteria).
EX-16	Has heart failure of Class III or IV (New York Heart Association criteria).
EX-17	Has sensory or motor neuropathy of Grade 4 (NCI CTCAE v4.03 criteria).
EX-18	Has other significant medical conditions (chronic or active within the past 6 months), including, but not limited to: cardiac disease (e.g., unstable angina, myocardial infarction, ventricular arrhythmia); uncontrolled seizure disorder; liver disease; or uncontrolled diabetes.
EX-19	Has any other condition that would, in the opinion of the Investigator, potentially compromise the safety or compliance of the patient or may preclude the patient's successful completion of the clinical trial.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

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Listing 16.2.2.3

Listing of Inclusion/Exclusion Criteria Not Met

Dose Group	Patient Number	IN/EX Criteria Not Met	Waiver Granted	Waiver Details	Comments
			Yes		
			No		

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Listing 16.2.2.4

Intent-To-Treat Patients Excluded from Per-Protocol Population

Dose Group	Patient Number	Reason for Exclusion

Note: This listing presents only subjects who are removed from the per-protocol population.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

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Listing 16.2.3

Protocol Deviations

Dose Group	Patient Number	Date of Deviation	Rel Day [1]	Category of Deviation	Deviation Specifics	Comments
				Inclusion / Exclusion Criteria Not Met		
				Prohibited Medication Taken		
				Blood Specimen Collection Missed / Out of Window		
				Other Protocol Procedure Missed / Out of Window		
				IMO-8400 Dose Missed		
				Other		

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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DATE: DDMMMYYYY HH:MM

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Listing 16.2.4.1

Demographic Characteristics

Dose Group	Patient Number	Informed Consent Date	Protocol Version Date	Date of Birth	Age (Years)	Gender	Of Child-bearing Potential	Race	Ethnicity
						Male	Yes	American Indian or Alaska Native	Hispanic or Latino
						Female	No	Asian	Not Hispanic or Latino"
								Black	
								Native Hawaiian or Other Pacific Islander	
								White	
								Other	

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: Concatenate specifics if “other” is chosen for race (Other: Specify).

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Listing 16.2.4.2

Medical History

Dose Group	Patient Number	System	Disease/ Procedure	Start Date	End Date	Ongoing at Screening?
						Yes
						No

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

DATE: HH:MM/DDMMMYYYY

Programming note: if Ongoing = Yes, mark ONGOING in end date column.

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Listing 16.2.4.3A

Waldenström's Macroglobulinemia Disease History – Part 1

Dose Group	Patient Number	Date of Diagnosis	Date of first treatment for WM	Experienced treatment-related AEs in past 3 months	Subject has been hospitalized in the past year
				Yes	Yes
				No	No

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Listing 16.2.4.3B

Waldenström's Macroglobulinemia Disease History – Part 2

			AEs in the past 3 months				Hospitalizations in the past year	
Dose Group	Patient Number	Experienced treatment-related AEs in past 3 months	Event Term	Start Date	End Date	Subject has been hospitalized in the past year	Date of Discharge	Discharge Diagnosis
		Yes				Yes		
		No				No		

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: if Ongoing = Yes, mark ONGOING in end date column.

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Listing 16.2.4.4

Prior Waldenström's Macroglobulinemia Therapy

Dose Group	Patient Number	Agent/ Treatment	Start Date	Stop Date	Best Clinical Response	Reason for Discontinuation	AEs experienced with this treatment

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Listing 16.2.4.5

MyD88 L265P Mutation Status

Dose Group	Patient Number	MyD88 L265P Mutation Status
		Present
		Absent

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

DATE: DDMMMYYYY HH:MM

Programming note: This data to come from an external source, and is not entered into the database.

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Listing 16.2.5.1

Study Drug Exposure

Dose Group	Patient Number	Cycle	Week	Both Doses Admin-istered	Injection	Location	Date/ Time	Rel Day [1]	Site	Volume Dispensed (unit)	Entire Dose Administered	Cum-ulative dose (mg) [2]
				Yes	First	Site					Yes	
				No	Second	Home Visit					No: [Specify]	

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] Cumulative dose is the volume dispensed multiplied times the number of injections.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: if Site = "Other", concatenate specifics, "Other Injection Site"
Programming note: If entire dose not administered, concatenate specifics "Please explain why entire dose was not administered."

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Listing 16.2.5.2

Pharmacokinetic Concentrations

Dose Group	Patient Number	Collection Date	Rel Day [1]	Time Point	Collection Time	Relative Time [2]	Drug Concentration (unit)

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] Relative time is calculated with respect to the time of each dose.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

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Listing 16.2.5.3

Pharmacokinetic Parameters

					Parameter				
Dose Group	Patient Number	Collection Date	Rel Day [1]	Time Point	Maximum Conc. (mg/ml)	Time to Maximum Conc. (hr)	AUC last (hr*mg/mL)	AUC Infinity (hr*mg/ml)	RA (AUC)

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] Relative time is calculated with respect to the time of each dose.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

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Listing 16.2.6.1

Disease Response

Dose Group	Patient Number	Date of Assessment	Rel Day [1]	Parameter	Clinical Response	Comments	Overall Response [2]
				Serum Monoclonal IgM	CR		
				Bone Marrow Histology	VGPR		
				Adenopathy	PR		
				Organomegaly	MR		
				Cytopenias	SD		
				Symptoms	PD		
					NE		
					Delayed Response		
					NA		

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] Overall Response derived from data entered onto the Disease Assessment eCRF based on the VIth International Workshop on Waldenström's Macroglobulinemia (Owen et al, 2012).
Note: CR = Complete response. VGPR = Very good partial response. PR = Partial response. MR = Minor response. SD = Stable disease. PD = Progressive disease. NE = Not evaluable. NA = Not applicable.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming Note: Overall Response retrieved from external data source, Excel spreadsheet from Idera.

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Listing 16.2.6.2A

Disease Assessment – Part 1

					Physical assessment of lymphadenopathy				Physical assessment of hepatomegaly		
Dose Group	Patient Number	Clinical Assessments Completed	Date of Assessment	Rel Day [1]	Results	Region	Size (unit)	Tenderness	Results	Abnormality	Clinically Significant
		Yes			Normal			None	Normal		Yes
		No			Abnormal			Mild	Abnormal		No
					Not Done			Moderate	Not Done		
								Severe			

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

DATE: DDMMMYYYY HH:MM

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Listing 16.2.6.2B

Disease Assessment – Part 2

Dose Group	Patient Number	Clinical Assessments Completed	Date of Assessment	Rel Day [1]	Physical assessment of splenomegaly			
					Results	Enlarged	Palpable	Tenderness
		Yes			Normal	Yes	Yes	None
		No			Abnormal	No	No	Mild
					Not Done			Moderate
								Severe

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

DATE: DDMMMYYYY HH:MM

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Listing 16.2.7.1

Adverse Events by Patient and MedDRA System Organ Class / Preferred Term

Dose Group:

Patient Number	SOC	Preferred Term	Onset Date/ Time	Onset Rel Day [1]	End Date/ Time	End Rel Day [1]	Sever- ity [2]	Serious	Rela- tionship [3]	Action Taken with IMO-8400	Action Taken for AE	Sequelae at Resolution
								Yes				Yes
								No				No

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] 1 = Grade 1: Mild. 2 = Grade 2: Moderate. 3 = Grade 3: Marked. 4 = Grade 4: Extreme. 5 = Grade 5: Death.
[3] Relationship to Study Drug: Prob Rel = Probably Related, Poss Rel = Possibly Related, Unlike Rel = Unlikely Related, Not Rel = Not related.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If sequelae at resolution, concatenate specifics (Yes: Specify sequelae).

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Listing 16.2.7.2

Adverse Events by MedDRA System Organ Class and Preferred Term

System Organ Class:

			Onset		End							
Preferred Term	Dose Group	Patient Number	Date/ Time	Rel Day [1]	Date/ Time	Rel Day [1]	Sever- ity [2]	Serious	Rela- tionship [3]	Action Taken with IMO-8400	Action Taken for AE	Sequelae at Resolution
								Yes				Yes
								No				No

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] 1 = Grade 1: Mild. 2 = Grade 2: Moderate. 3 = Grade 3: Marked. 4 = Grade 4: Extreme. 5 = Grade 5: Death.
[3] Relationship to Study Drug: Prob Rel = Probably Related, Poss Rel = Possibly Related, Unlike Rel = Unlikely Related, Not Rel = Not related.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If sequelae at resolution, concatenate specifics (Yes: Specify sequelae).

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Listing 16.2.7.3

Glossary of Adverse Event Verbatim Terms by MedDRA System Organ Class, Preferred Term, and Patient

MedDRA				
SOC	Preferred Term	Dose Group	Patient Number	Investigator Reported Term

Programming Note: Sort the listing by SOC, PT, Verbatim, Dose Group, and Patient Number.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

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Listing 16.2.7.4

Injection Site Reaction Assessments

Dose Group	Patient Number	Visit of Assessment	Date of Assessment	Rel day [1]	Time of Assessment	Visit of Injection	Site of Injection	Any ISR Reported
								Yes
								No

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
Note: If there was no injection site reaction noted, then further data was not recorded.
Ery=Erythema, Ind=Induration, Tend=Tenderness, Prur=Pruritus.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming Note: Put the definitions of the severity gradation on the first page.

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Listing 16.2.7.5

Patient Reported Injection Site Reactions

Dose Group	Patient Number	Date of Assessment	Rel Day [1]	Trait	Date of Onset	Rel day [1]	Date of Resolution	Rel Day [1]	Severity	Reaction ongoing at time of assessment	Sequelae	ISR Treated
										Yes		
										No		

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If ISR treated, concatenate specifics for con med or other treatment.

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Listing 16.2.7.6

Observed Injection Site Reactions

Dose Group	Patient Number	Date of Assessment	Rel Day [1]	Trait	Status	Severity	Size (mm)	ISR Treated	Previous ISRs for same site	Sequelae
				Erythema	Present	Grade 1			Yes	Yes: Specify
				Induration	Absent	Grade 2			No	No
				Tenderness		Grade 3				
				Pain		Grade 4				
				Pruritus		Grade 5				
				Blister		NA				
				Ulceration						
				Necrosis						

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
Note: NA = Not applicable

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If ISR treated, concatenate specifics for con med or other treatment. If sequelae = yes, concatenate specifics.

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Listing 16.2.8.1A

Laboratory Results: Hematology – Part 1

Dose Group: [Description]

Patient Number	Date/Time of Collection	Rel Day [1]	WBC Count (unit)	RBC Count (unit)	Hemo-globin (unit)	HCT (unit)	Platelet Count (unit)	MCH (unit)	MCHC (unit)	MCV (unit)

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
Note: HCT = Hematocrit, RBCs = Red Blood Cells, MCH = Mean Corpuscular Hemoglobin, MCHC = Mean Corpuscular Hemoglobin Concentration, MCV = Mean Corpuscular Volume, WBC = White Blood Cells.
Note: LP - Low Panic, L - Low Normal, H - High Normal, HP - High Panic, AB – Abnormal.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming Note: In all tables include SI parameters under the lab parameter.

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Listing 16.2.8.1B

Laboratory Results: Hematology – Part 2

Dose Group: [Description]

Patient Number	Date/Time of Collection	Rel Day [1]	Neutro-phils (unit)	Eosino-phils (unit)	Baso-phils (unit)	Lympho-cytes (unit)	Mono-cytes (unit)

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
Note: LP - Low Panic, L - Low Normal, H - High Normal, HP - High Panic, AB – Abnormal.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming Note: In all tables include SI parameters under the lab parameter.
Programming Note: In all tables include SI parameters under the lab parameter.

Repeat for:
- Listing 16.2.8.2 Laboratory Results: Chemistry
- Listing 16.2.8.3 Laboratory Results: Urinalysis
- Listing 16.2.8.4 Laboratory Results: Coagulation

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Listing 16.2.8.5

Laboratory Results: Serology

Dose Group	Patient Number	Date/Time of Collection	Rel Day [1]	HBsAg	HIV	HCV

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
Note: HBsAg = Hepatitis B surface antigen, HIV = Human immuno deficiency virus, HCV = Hepatitis C virus.

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Listing 16.2.8.6

Urine Pregnancy Test Results

Dose Group	Patient Number	Age	Date/Time Sample Collected	Rel Day [1]	Result of Pregnancy Test

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.8.7

Bone Marrow Biopsy

Dose Group	Patient Number	Date Sample Collected	Rel Day [1]	HBsAg	HIV	HCV

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
Note: HBsAg = Hepatitis B surface antigen. HIV = Human immuno deficiency virus. HCV = Hepatitis C virus.

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Listing 16.2.8.8

Serum Cytokines Test

Dose Group	Patient Number	Date of Collection	Rel Day [1]	IL-6 (unit)	IL-12 (unit)	IL-17 (unit)	IP-10 (unit)

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.8.9

Immunoglobulin (IgM) Results

Dose Group	Patient Number	Date of Collection	Rel Day [1]	Monoclonal IgM (unit)	Total IgM (unit)

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.8.10

Serum Antibody Results

Dose Group	Patient Number	Visit	Date of Collection	Rel Day [1]	Presence of Antibody to IMO-8400

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.9.1

Vital Signs

Dose Group	Patient Number	Date of Assessment	Rel Day [1]	Time-point	Height (cm)	Weight (kg)	SBP (mmHg)	DBP (mmHg)	Heart Rate (beats/min)	Respiratory Rate (beats/min)	Temperature (°C)	Any Abnormal, CS Results?

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
Note: Clinically significant results are represented by '*' after the result.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

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Listing 16.2.9.2

Physical Examination Findings

Dose Group	Patient Number	Date of Assessment	Rel Day [1]	Timepoint	Body System	Findings

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

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Listing 16.2.9.3

Eastern Cooperative Oncology Group (ECOG) Performance Status

Dose Group	Patient Number	Visit	ECOG Performance Status Assessed	Date of Assessment	Rel Day [1]	ECOG Score
			Yes			
			No			

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

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Listing 16.2.9.4

12-Lead Electrocardiogram Interval and Overall Assessment

Dose Group:

Patient Number	Date/Time of Assessment	Rel Day [1]	Ventricular Rate (bpm)	RR Interval (msec)	PR Interval (msec)	QRS Interval (msec)	QT Interval (msec)	QTc Interval (msec)	QTc Interval Method	ECG Result

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
Note: If QT interval available, then QTc-Fridericia calculated. If not, then QTc Interval and Method taken from ECG Strip.
ECG Result: NL = Normal; Ab-NCS = Abnormal, Not Clinically Significant; Ab-CS = Abnormal, Clinically Significant.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: QTc calculated by site and entered into the eCRF.

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Listing 16.2.9.5

12-Lead Electrocardiogram – Comments on Abnormal Assessments

Dose Group:

Patient Number	Date/Time of Assessment	Rel Day [1]	ECG Result	Comments

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
ECG Assessment: NL = Normal; Ab-NCS = Abnormal, Not Clinically Significant; Ab-CS = Abnormal, Clinically Significant.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

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Listing 16.2.9.6

Concomitant Medications

Dose Group	Patient Number	Start Date/ Rel Day [1]	End Date/ Rel Day [1]	Medication	Dose	Unit	Route	Frequency	Used to treat an AE	AE #

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
Note: BID = Twice a day, TID = Three times a day, QID = Four times a day, QD = Once a day, QOD = Every other day, QWK = Every week, Q2WK = Once every 2 weeks, Q3WK = Once every 3 weeks, QH = Every hour, Q4H = Every 4 hours, Q6H = Every 6 hours, OTO = One time only, PRN = As needed.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If medication is ongoing, enter ONGOING in end date column. If other is selected for unit, route, or frequency, concatenate specifics (Other: Specify).

9. REVISION HISTORY

Not applicable; this is the first draft of the SAP.

10. APPENDICES

10.1. Appendix 1: Evaluation of Response to Treatment and Disease Status

Table 10-1 summarizes the criteria for response to treatment. The full text of the VIth International Workshop classification (Owen et al 2008) is provided below, in Section 10.2.

Table 10-1 Summary of Evaluation of Response to Treatment and Disease Status

Parameter	Response				Stable Disease (SD)	Progressive Disease (PD)
	Complete (CR)	Very Good Partial (VGPR)	Partial (PR)	Minor (MR)		
Serum Monoclonal IgM[a]	Absent[e]	≥90% reduction	≥50% reduction	≥25% to <50% reduction	<25% reduction to <25% increase	≥25% increase
Bone Marrow histology	Absence of malignant cells	NA	NA	NA	NA	NA
Adenopathy, Organomegaly[b]	Resolved by CT	Resolved by CT	≥50% decrease by CT	NA	No progression	Progression
Cytopenias[c]	None	None new	None new	None new	None new	Progression
Symptoms[d]	None	None new	None new	None new	None new	Progression

NA =Not applicable.
a. Quantitative assessment by protein electrophoresis with immunofixation.
b. If present at baseline on CT.
c. Cytopenias: anemia, thrombocytopenia, leukopenia
d. Symptoms: unexplained recurrent fever ≥38.4°C, drenching night sweats, ≥10% weight loss, neuropathy, symptomatic hyperviscosity, or symptomatic cryoglobulinemia.
e. Must be confirmed ≥6 weeks later with a second serum immunofixation assay.
f. PD based on ≥25% increase in serum monoclonal IgM from nadir; must be confirmed by a second measurement.

The Third International Workshop for WM also defined the following categories (Kimby et al 2006).

Not evaluable response: Reserved for situations in which there is insufficient data for a determination of response to treatment.

Delayed response: A delayed response is described particularly after treatment with purine analogue or monoclonal antibody. The recommendation was that patients should be followed for at least 12 weeks after treatment initiation to be considered unresponsive to therapy.

10.2. Appendix 2: Classification of Disease Response for Waldenström's Macroglobulinemia

Reproduced from Reference Owen et al 2008.

Table I. Categorical response definitions.

Response category	Definition
Complete response (CR)	Absence of serum monoclonal IgM protein by immunofixation Normal serum IgM level Complete resolution of extramedullary disease, i.e., lymphadenopathy and splenomegaly if present at baseline Morphologically normal bone marrow aspirate and trephine biopsy
Very good partial response (VGPR)	Monoclonal IgM protein is detectable $\geq$ 90% reduction in serum IgM level from baseline* Complete resolution of extramedullary disease, i.e., lymphadenopathy/splenomegaly if present at baseline No new signs or symptoms of active disease
Partial response (PR)	Monoclonal IgM protein is detectable $\geq$ 50% but<90% reduction in serum IgM level from baseline* Reduction in extramedullary disease, i.e., lymphadenopathy/splenomegaly if present at baseline No new signs or symptoms of active disease
Minor response (MR)	Monoclonal IgM protein is detectable $\geq$ 25% but<50% reduction in serum IgM level from baseline* No new signs or symptoms of active disease
Stable disease (SD)	Monoclonal IgM protein is detectable <25% reduction and <25% increase in serum IgM level from baseline* No progression in extramedullary disease, i.e., lymphadenopathy/splenomegaly No new signs or symptoms of active disease
Progressive disease (PD)	$\geq$ 25% increase in serum IgM level* from lowest nadir (requires confirmation) and/or progression in clinical features attributable the disease

*Sequential changes in IgM levels may be determined either by M protein quantitation by densitometry or total serum IgM quantitation by nephelometry.

STATISTICAL ANALYSIS PLAN

Phase 1/2 Open-label, Multiple-dose, Dose-escalation Study to Evaluate the Safety and Tolerability of IMO-8400 in Patients with Relapsed or Refractory Waldenström's Macroglobulinemia

Protocol Number:	8400-401
Protocol Version and Date:	Version 7.0, 14 March 2016 Version 6.0, 13 August 2015 Version 5.0, 25 February 2015 Version 4.0, 22 Sep 2014 Version 3.0, 23 Jul 2014 Version 2.0, 18 Nov 2013 Version 1.0, 11 Oct 2013
Name of Test Drug:	IMO-8400
Phase:	Phase 1/2
Methodology:	Open-label, Multiple-dose, Dose-escalation, Multicenter
Sponsor:	Idera Pharmaceuticals, Inc. 167 Sidney Street Cambridge, MA 02139
Sponsor Representatives:	Julie Brevard, MPH Director of Statistics Idera Pharmaceuticals, Inc. Mark Cornfeld, MD, MPH Vice President & Medical Lead, Oncology Idera Pharmaceuticals, Inc.
Statistical Analysis Plan Date:	21 April 2017
Statistical Analysis Plan Version:	Final Version 2.0

DCM 04 May 2017 (pg # update in publishing)

APPROVAL SIGNATURE PAGE

Protocol Title:	Phase 1/2 Open-label, Multiple-dose, Dose-escalation Study to Evaluate the Safety and Tolerability of IMO-8400 in Patients with Relapsed or Refractory Waldenström's Macroglobulinemia
Sponsor:	Idera Pharmaceuticals, Inc. 167 Sidney Street Cambridge, MA 02139
Protocol Number:	8400-401
Document Date / Version:	21 April 2017 / Final Version 2.0

Veristat, LLC. Author:

Debora Manning, MPH
Biostatistician II
Veristat, LLC
118 Turnpike Road
Southborough, MA 01772

Signature: Debra Manning

Date: 27 APR 2017

Sponsor Approval

By signing this document, I acknowledge that I have read the document and approve of the planned statistical analyses described herein. I agree that the planned statistical analyses are appropriate for this study, are in accordance with the study objectives, and are consistent with the statistical methodology described in the protocol, clinical development plan, and all applicable regulatory guidances and guidelines.

I have discussed any questions I have regarding the contents of this document with the biostatistical author.

I also understand that any subsequent changes to the planned statistical analyses, as described herein, may have a regulatory impact and/or result in timeline adjustments. All changes to the planned analyses will be described in the clinical study report.

Sponsor Signatory:

Julie Brevard, MPH
Director of Statistics
Idera Pharmaceuticals, Inc.

Signature: Julie Brevard

Date: 27 APR 2017

TABLE OF CONTENTS

Section **Page**

TABLES INCLUDED IN THE TEXT

LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Definition
AE	Adverse Event
ATC	Anatomic Therapeutic Class
BMI	Body Mass Index
CR	Complete Response
CSR	Clinical Study Report
DLT	Dose Limiting Toxicity
DME	Dose Modifying Event
DRC	Data Review Committee
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EE	Efficacy Evaluable
EOS	End-of-Study
EOT	End-of-Treatment
ICH	International Conference on Harmonization
IgM	Immunoglobulin M
IRB	Institutional Review Board
ISR	Injection Site Reaction
ITT	Intent-to-Treat
MedDRA	Medical Dictionary for Regulatory Activities
MR	Minor Response
MTD	Maximum Tolerated Dose
MyD88	Myeloid differentiation primary response gene (88)
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
ORR	Objective Response Rate
PD	Progressive Disease
PK	Pharmacokinetics
PR	Partial Response
PT	Preferred Term
Rel Day	Relative Study Day
RP2D	Recommended Phase 2 dose
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SC	Subcutaneous
SD	Stable Disease (Standard deviation in statistical reference)
SI	International System of Units

Abbreviation	Definition
TEAE	Treatment-Emergent Adverse Event
TLR	Toll-Like Receptor
VGPR	Very Good Partial Response
WHO	World Health Organization
WM	Waldenström's Macroglobulinemia

1. STATISTICAL ANALYSIS PLAN OBJECTIVES

This statistical analysis plan (SAP) is designed to outline the methods to be used in the analysis of study data in order to answer the study objectives. Populations for analysis, data handling rules, statistical methods, and formats for data presentation are provided. The statistical analyses and summary tabulations described in this SAP will provide the basis for the results sections of the clinical study report (CSR) for this trial.

This SAP will also outline any differences in the currently planned analytical objectives relative to those planned in the study protocol.

2. INFORMATION FROM THE STUDY PROTOCOL

2.1. Introduction and Objectives

2.1.1. Introduction

Waldenström's Macroglobulinemia (WM) is a distinct B-cell lymphoproliferative disorder characterized by a lymphoplasmacytic infiltrate in the bone marrow and high levels of a monoclonal immunoglobulin M (IgM) in the serum (Dimopoulos et al, 2008). The disease can have a chronic, indolent course, with patients remaining asymptomatic for years. The principal complications include manifestations of the monoclonal gammopathy, including symptomatic hyperviscosity, cryoglobulinemia, and cold agglutinin disease; disease-related cytopenia; bulky adenopathy or organomegaly; severe neuropathy; amyloidosis; and disease transformation.

Many of the agents used in refractory or relapsing WM are cytotoxic or sharply immunosuppressive and have substantial safety risks in elderly patients that are characteristic of this disease. A novel targeted agent that provided a beneficial treatment effect with a better tolerability profile would address an unmet need in WM.

IMO-8400 is a second-generation oligonucleotide antagonist of Toll-like receptors (TLR) 7, 8 and 9, which blocks immune activation mediated through those receptors. In a Phase 1 study IMO-8400 was administered to healthy adults by subcutaneous (SC) injection at single-doses and multiple-doses (once weekly for 4 weeks) up to 0.6 mg/kg (see protocol Section 4.4.1 for details). All treatments were well-tolerated, with mild injection site reactions and no pattern of systemic reactions or laboratory changes.

In recent studies, a high frequency of mutation in the signaling pathway downstream of TLR7, 8 and 9 has been identified in patients with B-cell malignancies, including more than 90% of patients with WM (Treon et al, 2012). *In vitro* studies of B-cell tumor lines indicate that such mutations are associated with an increase in cell activation, proliferation and survival (Young and Staudt, 2013), and that loss of endosomal TLRs results in markedly decreased cell proliferation and survival (Lim, Barton, and Staudt, 2013). Data from Idera indicates that treatment of such cell lines with IMO-8400 has a similar effect. Further information about the preclinical and clinical characteristics of IMO-8400 may be found in the Investigator's Brochure.

The current study represents the first clinical trial of IMO-8400 in patients with B-cell malignancy.

2.1.2. Study Objectives

2.1.2.1. Primary Objective

The primary objective is to evaluate the safety and tolerability of escalating dose levels of IMO-8400 administered by SC injection in patients with relapsed or refractory WM.

2.1.2.2. Secondary Objectives

The secondary objectives are:

- To assess the treatment effect (clinical activity) of escalating dose levels of IMO-8400 using disease-specific international guidelines for classifying clinical response (Owen et al, 2012).
- To identify an optimal dose of IMO-8400 for further clinical evaluation.

- To characterize the pharmacokinetics of escalating dose levels of IMO-8400 administered by SC injection.

2.1.2.3. Exploratory Objectives

The exploratory objectives are:

- To investigate associations between the treatment effect of IMO-8400 and selected biomarkers (e.g., serum cytokines).
- To correlate the presence of myeloid differentiation primary response gene (88) L265P mutation with clinical outcome.
- To assess the potential immunogenicity of IMO-8400 administered by SC injection.

2.2. Study Design

2.2.1. Synopsis of Study Design

This is an open-label, multiple-dose, dose escalation study of IMO-8400 in patients with relapsed or refractory WM. The overall study design includes Part A, a dose escalation phase to investigate the safety and tolerability of planned dose levels of IMO-8400, and Part B, an expansion phase to further investigate the efficacy of the maximum tolerated dose (MTD)/ recommended Phase 2 dose (RP2D) identified in the escalation phase.

2.2.1.1. Part A: Dose-escalation

2.2.1.1.1. Dose-escalation Cohorts

The dose-escalation cohorts (3 to 6 patients each) will systematically evaluate the safety and tolerability of IMO-8400 at increasing dose levels in order to identify the MTD/RP2D. See Protocol Section 8 for further details on study treatment administration.

- The planned dose levels are IMO-8400 at 0.6, 1.2, 2.4, and 3.6 mg/kg administered once weekly and 1.2 mg/kg administered twice weekly (Table 2.1). Additional dose levels, schedules, and routes of administration will be evaluated based on the emerging data. Weekly exposure is based on body weight (measured at screening and the start of each cycle). Doses will be administered by SC injection.
- For Dose Level 3 (refer to Table 2.1), the total dose will be divided into 2 equal portions (1.2 mg/kg twice weekly), administered as separate SC injections over the course of the week, preferably 72 to 96 hours apart (minimum 48 hours).
- Once safety has been established for the 2.4 mg/kg/week as a divided weekly dose (1.2 mg/kg twice weekly), the same dose level of 2.4 mg/kg/week and subsequent dose levels will be given as a once weekly administration.
- Once the RP2D/MTD has been established, patients being treated at lower dose levels may have their doses escalated to the RP2D/MTD upon discussion and agreement between the Sponsor and the Investigator.

Table 2.1 Planned Dose Escalation Cohorts

Dose Level	IMO-8400 Dose (mg/kg)	Frequency	Initial Cohort Size
1 (starting dose)	0.6	Once Weekly	3-6
2	1.2	Once Weekly	3-6
3	1.2	Twice Weekly	3-6
4	2.4	Once Weekly	3-6
5	3.6	Once Weekly	3-6

2.2.1.1.2. Dose-escalation Procedures

Procedures for patient safety during dose-escalation are summarized below and presented in detail in the protocol sections and sections of this document indicated:

- Explicit definitions for identifying suspected adverse reactions as dose-limiting toxicity (DLT) events (see Section 2.2.5.1.1).
- Explicit definition for MTD (see Section 2.2.5.1.1).
- All injections of study medication will be administered by study personnel and all patients observed for 2 hours following the first injection (including the first injection of a new dose level in the case of intra-patient dose escalation) and for at least 30 min following all other injections.
- Detailed provisions for management of study drug in individual patients based on safety, tolerability, and disease response (see Section 2.2.2.1 and Protocol Section 6.5).
- Constitution of a Data Review Committee (DRC), comprised of the Idera Medical Monitor and Investigators from participating sites, to decide to continue or halt dose-escalation, or explore intermediate dose levels (see Section 2.2.3 and Section 2.2.5.1.1).

2.2.1.1.3. Dose-escalation Enrollment and Review

Each dose-escalation cohort is expected to enroll at least 3 patients, with a maximum of 6.

- If the initial 3 patients all complete 4 weeks of treatment without a DLT event, the DRC will conduct a dose-escalation review.
- If 1 of the initial 3 patients experiences a DLT event prior to completing 4 weeks of treatment, then enrollment at that dose level will continue to a total of 6 patients and the dose-escalation review will be done when all 6 patients have completed 4 weeks treatment.
- If 2 patients at a dose-level experience DLT events during the first 4 weeks of treatment, then no further patients will be enrolled until the DRC completes a review, which should be done as soon as feasible.

The DRC review will include all safety data available for the cohort. The following represent anticipated outcomes for the review process.

- Dose escalation – progression to the next planned dose level.

- Continue cohort enrollment (applicable only to review after 3 patients) – enroll up to 6 patients at the current dose level to obtain additional safety data for subsequent review.
- Dose de-escalation – enrollment of intermediate levels for exploration of other schedules of administration (see Section 2.2.5.1.1).
- Approve enrollment in the expansion cohort at that dose level, if applicable (see Section 2.2.1.2)
- No further dose escalation enrollment – at this time the DRC will indicate the dose level they consider represents the MTD.

2.2.1.2. Part B: Dose Expansion

2.2.1.2.1. Expansion Cohorts

The expansion cohorts provide for additional enrollment at agreed upon dose levels to assess the dose dependence of clinical response.

Once the MTD or potential RP2D and schedule have been established during dose escalation, up to 22 patients will be treated at the RP2D level according to this schedule. The Sponsor may decide at any point during the expansion phase to modify the RP2D based on emerging data including, but not limited to, safety, DLTs, pharmacokinetics (PK), and clinical activity. If such a change is made, enrollment may continue at the selected dose level in up to 22 patients.

2.2.2. Stopping Rules

The sponsor reserves the right to discontinue the study for safety or administrative reasons at any time. Should the study be terminated and/or the site closed for whatever reason, all documentation and study medication pertaining to the study must be returned to the sponsor or its representative.

If the trial is terminated prematurely or suspended, the Sponsor will promptly inform the participating Investigators and institutions, the regulatory authorities, and the Institutional Review Board (IRB) of the termination or suspension and the reason(s) for the action.

The maximum exposures to IMO-8400, the investigational agent in this study, will be as follows:

- Maximum number of patients: Approximately 60 patients in planned escalation and expansion cohorts; potential for additional patients in contingency cohorts or as replacements
- Maximum dose level: Undefined (pending dose escalation results) - The planned dose escalation cohort levels for IMO-8400 are 0.6, 1.2, 2.4, and 3.6 mg/kg administered once weekly and 1.2 mg/kg administered twice weekly
- Maximum treatment duration: Undefined (treatment is until study completion or until the patient experiences intolerable toxicity, disease progression, or withdraws consent, whichever comes first)

2.2.2.1. Stopping Rules for Individual Patients

In Protocol Versions <6, the duration of treatment is up to 24 weeks, with the option to extend treatment in the extension protocol, Study 8400-404. In Protocol Versions ≥6, treatment will continue until the patient experiences intolerable toxicity, disease progression, or withdraws consent, whichever occurs first.

Each enrolled patient will receive IMO-8400 at the assigned dose level until the earliest of:

- Clinical DLT event – see Section 2.2.5.1.1
- Disease progression – based on assessments at Week 1 of each cycle. Unscheduled assessments may be conducted in response to new clinical observations. Disease status will be classified according to international guidelines (Owen et al, 2012) (see Section 10.1 for details)
- Termination of participation in the study – due to adverse event (AE), withdrawal of consent, intolerable toxicity, or loss to follow up.

Study treatment will be discontinued for DLT clinical events and for disease progression (based on discussion between the Sponsor and Investigator – See Protocol Section 6.5.1). For DLT laboratory events and dose modifying events (DMEs; clinically significant toxicities or DLTs that occur after 5 weeks of treatment), provision is made for pausing treatment for up to 3 weeks and, if the acute toxicity improves sufficiently, resuming treatment at a lower dose level (see Protocol Section 6.5.2 for details). The Investigator will review with the Medical Monitor decisions to discontinue, pause, and/or start study treatment.

2.2.3. Data Review Committee (DRC)

The Data Review Committee will be comprised of the Idera Medical Monitor and Investigators from participating sites to decide whether to continue or halt dose escalation, or explore intermediate dose levels.

A patient will be considered evaluable for purposes of DRC review if they meet either of the following criteria:

- Received at least 1 dose of study drug and had treatment discontinued because of a DLT event as defined in Protocol Section 6.3.1 or
- Received all doses of study drug in the first 4 weeks of treatment and completed Week 5 assessment procedures.

2.2.4. Study Procedures

The schedule of assessments, as outlined in the study protocol, is provided in Table 2.2,The schedule is presented relative to the day and time of dosing. All Days are relative to the day of the first injection of study drug, designated Day 1. All weeks are relative to Week 1, defined as Day 1 through Day 7, inclusive. All times are relative to injection, designated 0 hr; “pre-dose” vital signs are to occur within 1 hour prior to injection; all other pre-dose procedures are to occur prior to injection on the same calendar day.

The screening evaluation may be performed up to 21 days prior to dosing.

Laboratory assessments for disease status will be conducted at Screening, every 4 weeks ± 1 week (Week 1 and Week 5 of each cycle), every 12 weeks ± 4 weeks during the Follow-up Phase, at the end-of-treatment (EOT) visit, and at the end-of-study (EOS) visit. Radiologic imaging and bone marrow biopsy will be performed at Screening and at EOT visit or as clinically indicated.

The criteria for response to treatment will be classified using disease-specific criteria as proposed by the VIth International Workshop on Waldenström’s Macroglobulinemia (Owen et al, 2012) (see Section 10.1).

Table 2.2 Schedule of Study Events

Visit[1]	Scrn[2]	Day 1	Treatment Period											EOT[3]	EOS[3]	Follow-up
Cycle			Cycle 1			Even Numbered Cycles				Odd Numbered Cycles						Every 12 weeks (± 4 weeks)
Week			2-4	5	6-8	1	2-4	5	6-8	1	2-4	5	6-8			
Evaluation																
Informed Consent[4]	X															Patients who discontinue for reasons other than progressive disease should be assessed per Response Assessment in WM[24] until documentation of progressive disease, start of new anti-cancer therapy, until the study ends, or for up to 6 months from the last patient's first treatment cycle, whichever one comes first.
Inclusion/ Exclusion	X															
Medical History[5]	X															
Cryoglobulin & Cold Agglutinin Lab Tests[6]																
Physical examination[8]	X	X	X[8]	X		X		X		X		X		X	X	
Body weight[7]	X	X				X				X				X	X	
Height measurement	X															
Vital signs[9,10]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Clinical assessment for Tumor Status[11]	X	X				X				X				X	X	
Total IgM & Monoclonal Protein Lab Tests[12]	X	X		X		X		X		X				X	X	
ECOG[7]	X	X				X				X				X	X	
CT or MRI imaging[13]	X													X		
Safety Laboratory Tests[14]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Urinalysis[7]	X	X		X		X		X		X		X		X	X	
12-lead ECG[15]	X	X[15]		X[15]		X[15]		X[15]		X[15]		X[15]		X		
Pregnancy test (females only)[16]	X					X				X				X	X	
Serology	X															
PK[17]		X				X				X				X	X	
Serum Cytokines[18]		X				X				X				X	X	
Antibodies to IMO-8400[18]		X				X				X				X	X	
Serum NF-κB[19]		X				X				X				X	X	
Initial Dx Bone Marrow Slides[20]	X															
Bone Marrow Biopsy& Aspirate[21]	X													X		
Assessment of Injection Site[22]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Study Drug Administration[10,23]		X	X	X	X	X	X	X	X	X	X	X	X			
AE & Concomitant Med Monitoring	From Screening to EOS Visit															

Abbreviations: AE=adverse event; CT=computed tomography; ECG=electrocardiogram; ECOG=Eastern Cooperative Oncology Group; EOS=end-of-study; EOT=end-of-treatment; IgM=immunoglobulin M; NF-κB=nuclear factor kappa-light-chain-enhancer of activated B cells; PK=pharmacokinetic; MRI=magnetic resonance imaging; Scrn=Screening; WM=Waldenström's macroglobulinemia

[1] Day 1 is the day of the first injection of study drug. All weeks for a given cycle are relative to the day of the first injection of study drug for that Cycle and are defined as Day 1 through Day 7, inclusive; all times are relative to injection, designated 0 hour; "pre-dose" vital signs are to occur within 1 hour prior to injection; all other pre-dose procedures are to occur prior to injection on the same calendar day.

[2] Screening procedures may be performed up to 21 days prior to Day 1.

[3] If treatment is terminated prematurely for any reason, the EOT visit will be performed within 5 days of the decision to terminate; the EOS visit will be performed 30 to 35 days after the last dose of study drug.

[4] Informed consent must be signed prior to all study-specific screening procedures.

[5] Medical history includes, but is not limited to, a detailed review of the patient's malignancy, prior treatments, relevant current or past abnormalities or diseases, and signs and symptoms of WM at baseline.

[6] Cryoglobulin and cold agglutinin laboratory testing to be performed at Screening (local laboratory).

[7] To occur pre-dose

[8] During Cycle 1 only, physical examination will be done on Week 2. In subsequent cycles, physical examinations will be done every 4 weeks.

[9] Vital signs comprise heart rate, blood pressure, respiratory rate and temperature. Vital signs will be obtained pre-dose (within 1 hour prior to injection) and post-dose at 30 (± 5) min after dosing. On Day 1 of Cycle 1, Week 1, post-dose vital signs will also be obtained at 2 hours (± 20 min).

[10] For patients who receive a second weekly dose, vital signs will be obtained pre-dose (within 1 hour prior to injection) and post-dose at 30 (± 5) min after dosing, and assessment of the injection site, as previously noted, will be conducted.

[11] Clinical assessment for tumor status will be conducted pre-dose on dosing visits and will include assessment for lymphadenopathy, hepatomegaly, and splenomegaly (see Protocol Section 9.4.1 for details).

[12] Assessments will be conducted pre-dose on dosing visits, and includes total serum IgM, monoclonal serum IgM, serum free light chains, urine free light chains, serum viscosity, and serum β2-microglobulin; see Protocol Section 9.4.2 for details.

[13] CT or MRI imaging of chest, abdomen, and pelvis with the same modality used for every assessment; see Protocol Section 9.4 for details.

[14] The full panel of safety laboratory tests (hematology, serum complement, chemistry and coagulation) will be done pre-dose on Day 1, and Weeks 1 and 5 of each cycle (including pre-treatment criteria presented in Protocol Section 8.4.1); a focused panel (hematology, selected chemistry) will be done pre-dose on Weeks 3 and 7 of each cycle; see Protocol Section 9.7.1 for details. Unscheduled tests to confirm decreases in serum complement levels will be performed (see Protocol Section 6.5.4).

[15] ECGs are to be performed pre-dose and 2 hours post-dose on Day 1 of Cycle 1 and pre-dose at the first dosing visit of Weeks 1 and 5 of each cycle thereafter. In addition, an ECG is to be performed at 2 hours post-dose on Day 1 of each odd-numbered cycle.

[16] Serum pregnancy testing will be done pre-dose and evaluated at the central laboratory.

[17] PK samples will be collected as scheduled in relation to the first dose administered on Day 1 of every cycle. Samples will be obtained pre-dose (within 1 hour prior to injection) and post-dose at 1 hour (± 5 min), 2 hours (± 10 min) and 4 hours (± 15 min) after dosing. PK samples will also be taken at EOT and EOS.

[18] Serum for cytokines and antibodies to IMO-8400 will be collected as scheduled in relation to the first dose administered on Day 1 of every cycle and will be obtained pre-dose (within 1 hour prior to injection).

[19] Serum samples for NF-κB analysis will be obtained pre-dose (within 1 hour prior to injection) and post-dose at 4 hours (± 15 min) (see Protocol Section 9.9 for details) and will be submitted to central laboratory.

[20] Bone marrow slides will be obtained from initial WM diagnosis.

[21] Bone marrow biopsy and aspirate will be collected at Screening, EOT, and to document complete response as appropriate (see Protocol Section 16.2) and submitted to central laboratory (see Protocol Sections 9.4.4 and 12.4.1). If patients have a bone marrow biopsy within 4 weeks of EOT, the biopsy will not be repeated at EOT. The Screening Visit sample will also be assayed for the MyD88 L265P mutation.

[22] Assessment of all prior injection site(s) with grading and measurement of any reaction (see Protocol Section 9.6.5). In addition, on dosing days, the planned injection site will be assessed to confirm it is appropriate for use.

[23] Schedule applies to all patients receiving once weekly dosing and to the first weekly dose for all patients receiving twice weekly dosing (see Protocol Sections 1.3.2 and 8.4 for details).

[24] Response assessment is summarized in Protocol Section 16.2 and includes total serum IgM, serum monoclonal IgM, bone marrow histology, adenopathy/organomegaly, cytopenias, and symptoms (see Protocol Section 9.5 for details). Total IgM and monoclonal protein lab tests (see Protocol Section 9.4.2 for details) will be submitted to central laboratory.

2.2.5. Safety, Efficacy, and Pharmacokinetic Parameters

2.2.5.1. Safety Parameters

The safety and tolerability of IMO-8400 will be assessed using reported and observed adverse events (AEs) as well as scheduled safety observations including vital signs, symptom review, physical examination, laboratory tests (hematology, serum complement, clinical chemistry, and coagulation), urinalysis, electrocardiograms (ECGs), and reported and observed ISRs. Additional unscheduled assessments will be performed at the Investigator's discretion.

Adverse events will be graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 4.03. Adverse Events will be coded using Medical Dictionary for Regulatory Activities (MedDRA) version 16.0 and tabulated by event, grade, and relationship to study therapy. Laboratory results, vital signs, and ECG parameters will be summarized using descriptive statistics. Laboratory values will also be graded according to NCI CTCAE, Version 4.03, and summarized using shift tables. Injection site reactions will be summarized by incidence and time-to-event analyses will be performed. Details for the injection site grading and the intensity scale for reporting ISR AEs are located in Section 10.2 and Section 10.3.

2.2.5.1.1. Definition of Dose Limiting Toxicity and Maximum Tolerated Dose

A DLT can be either a clinical or laboratory AE. A potential DLT event is defined as a treatment-emergent AE that meets *any* of the following criteria using NCI CTCAE v4.03 grading:

- Is a clinical event of Grade 3 or higher severity, except for the following:
  - Alopecia
  - Grade 3 fatigue
  - Grade 3 nausea/vomiting that has not been treated with optimal anti-emetic treatments
  - Grade 3 diarrhea that has not been treated with optimal anti-diarrheal treatments
  - AE related to the underlying disease
- Is a confirmed laboratory finding of Grade 3 or higher severity and has been assessed as related to IMO-8400 (any relationship other than "not related") with the exceptions of neutropenia and thrombocytopenia. DLTs with respect to neutropenia/thrombocytopenia are outlined below:
  - Grade 4 neutropenia lasting > 7 days
  - Grade 3 or 4 neutropenia with a sustained temperature > 101.3º F
  - Grade 3 thrombocytopenia associated with clinically significant bleeding that requires transfusion therapy
  - Grade 4 thrombocytopenia

Clinically significant toxicities or DLTs that occur after Week 5 of Cycle 1, are defined as DMEs and may be considered when determining the RP2D.

The DRC will review all potential DLT events to assess causality, i.e., relationship to study drug (related, possibly related, unlikely related, or not related). Events will be considered DLT events

unless they are unanimously assessed as "Not related", that is, a factor other than study drug is the cause of the event.

The MTD is the dose level meeting *both* of the following criteria:

- It is below the level at which 2 or more patients experienced DLTs during the first four weeks of treatment;
- It is a dose level at which no more than 1 patient experienced DLTs during the first four weeks of treatment.

The RP2D will be a dose at or below the MTD based on clinical data.

2.2.5.2. Efficacy Parameters

Overall disease response reported is investigator-assessed, using disease-specific international guidelines for classifying clinical response (Owen et al, 2012).

The primary treatment effect parameter is objective response rate (ORR), defined as the occurrence of complete response (CR), very good partial response (VGPR), partial response (PR), or minor response (MR), presented by dose level and overall.

Secondary efficacy endpoints include:

- The distribution of response classes identified by best overall response
- Time to progression – Time from initiation of treatment to the first documented evidence of disease progression, with deaths due to unrelated causes censored.
- Progression-free survival (PFS) – Time from the initiation of treatment to disease progression or death from any cause.
- Time to best observed response – Time from the initiation of treatment to the first occurrence of the best observed category of response.
- Percent and absolute change in quantitative serum levels of monoclonal and total IgM.

Exploratory endpoints include the following investigational factors, analyzed with regard to disease status:

- Presence or absence of MyD88 L265P and CXCR4 mutation in tumor cells
- Serum cytokine levels and change from baseline
- Serum levels of antibody to IMO-8400
- NF-κB inhibition
- Absolute change from baseline in hemoglobin and platelet levels

Additional exploratory analysis may be performed on additional endpoints of interest or subpopulations.

2.2.5.3. Pharmacokinetic Parameters

Details regarding PK parameters and analysis will be described in a separate PK SAP and report.

3. PATIENT POPULATION

3.1. Population Definitions

The following patient populations will be evaluated and used for presentation and analysis of the data:

Safety Population: All patients who received at least one dose of study treatment.

Efficacy Evaluable (EE) Population – all patients who completed ≥1 cycle of therapy (i.e. at least 8 weeks of at least one dose of treatment) or those who discontinued due to progressive disease or DLT.

3.2. Protocol Deviations

For protocol deviations relating to individual patients, the event and relevant circumstances will be recorded on source documents and on the appropriate electronic case report form (eCRF). Protocol deviations will be determined and documented prior to database lock.

All protocol deviations will be presented in a data listing.

Relevant Output

Listing 16.2.2.2 Protocol Deviations

4. GENERAL STATISTICAL METHODS

4.1. Sample Size Justification

Consistent with the primary objective, the study design represents a pragmatic assessment of safety and tolerability across different dose levels of IMO-8400 based upon clinical evaluations and laboratory tests.

Following identification of the MTD/RP2D, up to an additional 22 patients will be enrolled at the MTD or proposed RP2D level. With a total sample size of 22 patients, there is a 90% probability to detect an AE with a true incidence rate of 10%. A secondary objective of this study is to determine the treatment effect of IMO-8400 in patients enrolled at the MTD/RP2D. Using the exact binomial distribution with a 1-sided test and an alpha of 0.05, there is 79% power to detect a response rate of 33% as compared to a null response rate of 10%.

4.2. General Methods

All data listings that contain an evaluation date will contain a relative study day (Rel Day). Relative study days are defined as follows:

- Rel Day 1 is defined as the calendar day of the first injection of study drug.
- The days prior to Rel Day 1 are designated Rel Day –1, Rel Day –2, etc; there is no Rel Day 0.
- The days following the day of the first injection of study drug are designated Rel Day 2, Rel Day 3, etc.
- The times of events related to dosing of study drug will be designated as minutes or hours before or after the time of dosing (i.e., the subcutaneous injection of study drug), which is designated as t = 0 (zero). Thus, 15 minutes prior to dosing is t = –15 min; 2 hour after dosing is designated t = 2 h.

All output will be incorporated into Microsoft Word files, sorted and labeled according to the International Conference on Harmonisation (ICH) recommendations, and formatted to the appropriate page size(s).

Tabulations will be produced for appropriate demographic, baseline, efficacy, and safety parameters. For categorical variables, summary tabulations of the number and percentage of patients within each category (with a category for missing data) of the parameter will be presented. For continuous variables, the number of patients, mean, median, standard deviation, minimum, and maximum values will be presented. For some efficacy parameters, a confidence interval will also be presented, as described in Section 5.

Data will be listed by patient and dose and summarized by dose and overall. All data will be included in summary tabulations.

4.3. Computing Environment

All descriptive statistical analyses will be performed using SAS statistical software Version 9.3 or above, unless otherwise noted.

4.4. Baseline Definitions

For all measures, baseline will be defined as the most recent measurement prior to the first administration of study drug.

4.5. Methods of Pooling Data

Data will be pooled across all study sites. All IMO-8400 dosed patients will be pooled together and presented separately by dose level.

4.6. Adjustments for Covariates

Exploratory efficacy analyses for efficacy endpoints may be done by the presence or absence of relevant mutations (e.g. MyD88 L265P or CXCR4); the presence or absence of these mutations may be included in a model as a covariate if any modeling analyses are done.

4.7. Multiple Comparisons

No adjustments for multiple comparisons will be made. As the primary purpose of this study is to assess the safety and tolerability of IMO-8400, efficacy assessments are secondary and the type I error rate will not be adjusted.

4.8. Subpopulations

Efficacy analyses may be done on the subpopulation of ibrutinib-refractory patients. Select efficacy laboratory parameters will be summarized for the subpopulation of patients who have not received a transfusion during the course of the study.

4.9. Withdrawals, Dropouts, Loss to Follow-up

A patient who does not meet the criteria for "evaluable" as explained above in Section 2.2.3 may be replaced to assure the requirements for completing the cohort are met. Replacement patients will be identified by distinctive patient numbers and will receive the same dose level as the patient being replaced.

4.10. Missing Data

Missing data will not be imputed, except as described in this section. All the data recorded on the eCRF will be included in data listings that will accompany the CSR.

When tabulating AE data, partial dates will be imputed as follows. If the day of the month is missing, the onset day will be set to the first day of the month unless it is the same month and year as study treatment. In this case, to conservatively report the event as treatment-emergent, the onset date will be assumed to be the first date of treatment. If the onset day and month are both missing, the day and month will be assumed to be January 1, unless the event occurred in the same year as the study treatment. In this case, the event onset will be coded to the day of treatment in order to conservatively report the event as treatment-emergent. A missing onset date will be coded as the first day of treatment. Listings will present all data as reported (i.e., without imputations).

When tabulating time since initial diagnosis and time since most recent therapy for disease history, partial dates will be handled as follows. If the day of the month is missing, the day will be set to the last day of the month. If both the date and month are missing, the day and month will assumed to be December 31.

4.11. Visit Windows

It is expected that all visits should occur according to the protocol schedule; visits outside of this schedule will be listed as a protocol deviation. Visits occurring outside of the visit windows as described in the protocol schedule will be included in summary tabulations if corresponding to a scheduled visit. Unscheduled assessments will not be summarized in tabulations that present

data by visit. However, in shift tables or summaries of best response, data from unscheduled assessments will be included. All data will be provided in listings, including the relative day of all dates presented.

4.12. Interim Analyses

Interim safety data will be examined on an ongoing basis to ensure patient safety and to comply with the clinical trial dose escalation rules. There is no formal interim analysis planned for efficacy.

5. STUDY ANALYSES

5.1. Patient Disposition

Patient disposition will be tabulated and will include the number enrolled (i.e. treated) at each dose level, the number prematurely discontinued from treatment, the reason for discontinuation, and the number in each analysis population.

A by-patient data listing of study completion information including the reason for premature study withdrawal and premature treatment discontinuation will be presented. A by-patient data listing of inclusion/exclusion criteria not met will also be presented.

Relevant Output

Table 14.0.1	Treatment Codes Applicable to Tables and Listings
Table 14.1.1.1	Patient Enrollment and Disposition
Listing 16.2.1.1	Patient Disposition
Listing 16.2.1.2	End of Treatment (EOT) Visit Status
Listing 16.2.1.3	End of Study (EOS) Visit Status
Listing 16.2.2.1	Inclusion/Exclusion Criteria Not Met
Listing 16.2.3.1	Study Populations

5.2. Demographics and Baseline Characteristics

Demographics and baseline characteristics, including medical and disease history, will be summarized and presented by dose level and overall. Ethnicity, race, sex, age, height, weight, body mass index (BMI), baseline ECOG Performance Status, and presence or absence of MyD88 L265P or CXCR4 mutation in tumor cells will be summarized.

Disease history will include years since initial diagnosis, baseline International Prognostic Scoring System for WM (IPSSWM) category (low, med, high), and baseline values of the following laboratory parameters: total IgM, monoclonal IgM, hemoglobin, platelet count, and β2 microglobulin. Baseline signs and symptoms of WM will also be summarized.

The IPSSWM category is derived as follows:

1) Except for age, each of the below factors (at baseline) is worth a single point. The points are added to make a score, which is used to divide patients into 3 risk groups:
   a) Age more than 65 years old
   b) Blood hemoglobin level 11.5 g/dL or less
   c) Platelet count 100,000/mcL or less
   d) Beta-2 microglobulin more than 3 mg/L
   e) Monoclonal IgM level more than 7 g/dL
2) Using the points identified in step 1, the risk groups as assigned as follows:
   a) Low-risk = patients 65 or younger who have no more than 1 point
   b) Intermediate-risk = patients who are older than 65 with 2 or fewer points, and those 65 or younger who have 2 points
   c) High-risk = patients of any age who have at least 3 points

A summary of prior treatments will include number and percentage of patients who have received at least one prior therapy, including type of treatment, best overall response, and reason

for discontinuation of therapy. Number of prior therapies will be summarized both continuously and categorically (i.e., 1, 2, 3, or 4+ prior therapies). Number of days since most recent therapy will also be summarized.

Demographic, baseline, and medical history data for each patient will be provided in data listings.

Relevant Output

Table 14.1.2.1	Demographic Characteristics (Safety Population)
Table 14.1.2.2	Baseline Characteristics (Safety Population)
Table 14.1.3.1	Disease History and Baseline Disease Characteristics (Safety Population)
Table 14.1.4.1	Prior Treatments (Safety Population)
Table 14.1.5.1	Baseline Waldenström's Macroglobulinemia Symptoms (Safety Population)
Listing 16.2.4.1	Demographic Characteristics
Listing 16.2.4.2	Medical History
Listing 16.2.4.3	Waldenström's Macroglobulinemia Disease History
Listing 16.2.4.4	Prior Waldenström's Macroglobulinemia Therapy
Listing 16.2.4.5	Baseline Waldenström's Macroglobulinemia Symptoms
Listing 16.2.4.6	MyD88 L265P or CXCR4 Mutation Status
Listing 16.2.9.3	Eastern Cooperative Oncology Group (ECOG) Performance Status

5.3. Safety Analyses

Safety observations will be analyzed using descriptive statistics and tabulation. No formal statistical comparisons are planned. All safety data will be presented in listings.

5.3.1. Study Drug Exposure

Study drug exposure will be tabulated by the number of cycles of study drug received, where a completed cycle is defined at receiving 8 weeks of at least one dose of treatment for that cycle. The number and percentage of patients will be reported by dose group and overall.

Cumulative exposure to IMO-8400 (mg) will be summarized by dose group and overall, where cumulative exposure is the actual dose received summed across all visits. The actual dose for each injection will be calculated as follows:

Dose (mg) = [assigned dose (mg/kg) * volume administered (mL)] / concentration of 0.007 (mL/kg)

The total number of doses received will be summarized. The number of missed doses will also be tabulated, as well as the reason the dose was missed per patient (i.e. if a patient missed multiple doses for the same reason, they will only be counted once for that reason).

Dosing information for each patient will be presented in a data listing.

Relevant Output

Table 14.3.5.1	Study Drug Exposure (Safety Population)
Listing 16.2.5.1	Study Drug Exposure

5.3.2. Adverse Events

Adverse events will be coded using the MedDRA coding system and displayed in tables and data listings using system organ class (SOC) and preferred term.

Analyses of AEs will be performed for those events that are considered treatment-emergent, where treatment-emergent is defined as:

- any AE with onset after the first administration of study medication (Day 1) through the EOS visit,
- any AE that was present at baseline but worsened in intensity or was subsequently considered drug-related by the Investigator through the EOS visit, or
- any AE with missing onset date.

The incidence of treatment-emergent AEs (TEAEs) will be presented by individual and pooled dose levels. For each tabulation, TEAEs are summarized by patient incidence rates; therefore, in any tabulation, a patient contributes only once to the count for a given TEAE (SOC or preferred term), irrespective of the number of episodes of a particular TEAE term reported. No formal hypothesis-testing analysis of AE or TEAE incidence rates will be performed.

An overview summary of the number and percentage of patients with any TEAE, TEAE related to study drug, grade ≥3 TEAE, serious TEAE (SAE), DLT, TEAE leading to death, and TEAE leading to premature discontinuation of study treatment will be presented.

Additional summary tables by SOC and preferred term will be produced for the following:

- All TEAEs
- All TEAEs by relationship to study drug (drug-related, not drug-related) where drug-related AEs include events with probable, possible and missing relationships
- All non-serious TEAEs
- All serious TEAEs
- All TEAEs by highest severity grade (grade 1 or 2, grade 3, or grade ≥4)
- All DLTs

For each injection site, local ISRs will be summarized by the worst grade post-treatment for each symptom. Pain, tenderness, pruritus, and induration will be summarized using number and percentage of patients by toxicity grade and overall. Blisters, ulceration, erythema, and necrosis measurements (mm) will be summarized descriptively, including quartiles and 90^{th} percentiles, as well as categorically by grade. For each injection site the worst grade post treatment is counted per patient and symptom. In addition, each symptom will be summarized over time by visit and grade and overall.

All AEs occurring from the date of signed informed consent through the end of the study will be listed. Additionally, a glossary of AE verbatim terms by preferred term and SOC will be provided. A separate listing for system organ class complete name and their corresponding abbreviations will be provided.

By-patient listings will also be provided for the following: patient deaths, SAEs, DLTs, and TEAEs leading to premature discontinuation of study treatment.

Relevant Output

Table 14.3.1.1	Summary of Treatment-Emergent Adverse Events (Safety Population)
Table 14.3.1.2	Incidence of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term (Safety Population)
Table 14.3.1.3	Incidence of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term and Strongest Relationship to Study Drug (Safety Population)
Table 14.3.1.4	Incidence of Non-Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term (Safety Population)
Table 14.3.1.5	Incidence of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term (Safety Population)
Table 14.3.1.6	Incidence of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term and by Highest Grade (Safety Population)
Table 14.3.1.7	Incidence of Dose-Limiting Toxicity Adverse Events by MedDRA System Organ Class and Preferred Term (Safety Population)
Table 14.3.1.8	Incidence of Observed Local Injection Site Reactions by Worst Grade Post Baseline (Safety Population)
Table 14.3.1.9	Incidence of Observed Local Injection Site Reactions by Worst Grade and Scheduled Visit (Safety Population)
Table 14.3.2.1	Listing of Adverse Events Leading to Death
Table 14.3.2.2	Listing of Serious Adverse Events
Table 14.3.2.3	Listing of Dose Limiting Toxicities
Table 14.3.2.4	Listing of Premature Treatment Discontinuations Due to Adverse Events
Listing 16.0.1	System Organ Class Abbreviations
Listing 16.2.7.1	Adverse Events by Patient and System Organ Class / Preferred Term
Listing 16.2.7.2	Adverse Events by System Organ Class / Preferred Term
Listing 16.2.7.3	Glossary of Adverse Event Verbatim Terms by MedDRA System Organ Class, Preferred Term, and Patient
Listing 16.2.7.4	Injection Site Reaction Assessments
Listing 16.2.7.5	Patient Reported Injection Site Reactions
Listing 16.2.7.6	Observed Injection Site Reactions

5.3.3. Laboratory Data

Clinical laboratory values will be reported in US units.

This study collects central laboratory data, but in some instances local laboratory data may be collected. Local laboratory data will not be summarized but it will be included in the laboratory listings. The final central laboratory data will not be incorporated into the electronic data capture (EDC) system; the data, including the normal laboratory ranges, will be in Excel format sent directly from the central laboratory. The local laboratory data will be incorporated into the EDC system, but local laboratory ranges will be collected externally in Excel format.

The actual value and change from baseline to each scheduled evaluation will be summarized for hematology, chemistry, coagulation, and serum complement parameters.

Laboratory CTCAE grades shift from baseline to the worst grade post baseline will be tabulated for individual and pooled dose groups using number and percentage of patients. These comparisons will include values from unscheduled visits.

All laboratory data will be provided in data listings, including cryoglobulins, cold agglutinins, serology, and pregnancy test data, separately for local and central laboratory results. Out of range values will be flagged as H or L, corresponding to high or low. Local laboratory listings will flag values that are considered to be clinically significant by the investigator.

Relevant Output:

Table 14.3.5.2A	Summary and Change from Baseline for Hematology Parameters by Scheduled Visit and Dose Group (Safety Population)
Table 14.3.5.2B	Summary and Change from Baseline for Chemistry Parameters by Scheduled Visit and Dose Group (Safety Population)
Table 14.3.5.2C	Summary and Change from Baseline for Coagulation Parameters by Scheduled Visit Point and Dose Group (Safety Population)
Table 14.3.5.2D	Summary and Change from Baseline for Serum Complement Parameters by Scheduled Visit and Dose Group (Safety Population)
Table 14.3.5.3A	Shifts from Baseline to Worst CTCAE Grade Post-Baseline in Hematology Parameters by Dose Group (Safety Population)
Table 14.3.5.3B	Shifts from Baseline to Worst CTCAE Grade Post-Baseline in Chemistry Parameters by Dose Group (Safety Population)
Table 14.3.5.3C	Shifts from Baseline to Worst CTCAE Grade Post-Baseline in Coagulation Parameters by Dose Group (Safety Population)
Listing 16.2.8.1A	Central Laboratory Results: Hematology – Part 1
Listing 16.2.8.1B	Central Laboratory Results: Hematology – Part 2
Listing 16.2.8.1C	Local Laboratory Results: Hematology – Part 1
Listing 16.2.8.1D	Local Laboratory Results: Hematology – Part 2
Listing 16.2.8.2A	Central Laboratory Results: Chemistry – Part 1
Listing 16.2.8.2B	Central Laboratory Results: Chemistry – Part 2
Listing 16.2.8.2C	Central Laboratory Results: Chemistry – Part 3
Listing 16.2.8.2D	Local Laboratory Results: Chemistry – Part 1
Listing 16.2.8.2E	Local Laboratory Results: Chemistry – Part 2
Listing 16.2.8.2F	Local Laboratory Results: Chemistry – Part 3
Listing 16.2.8.3A	Central Laboratory Results: Urinalysis – Part 1
Listing 16.2.8.3B	Central Laboratory Results: Urinalysis – Part 2
Listing 16.2.8.3C	Central Laboratory Results: Urinalysis – Part 3
Listing 16.2.8.3D	Central Laboratory Results: Urinalysis – Part 4
Listing 16.2.8.3E	Central Laboratory Results: Urinalysis – Part 5
Listing 16.2.8.3F	Local Laboratory Results: Urinalysis – Part 1
Listing 16.2.8.3G	Local Laboratory Results: Urinalysis – Part 2
Listing 16.2.8.3H	Local Laboratory Results: Urinalysis – Part 3
Listing 16.2.8.4A	Central Laboratory Results: Coagulation
Listing 16.2.8.4B	Local Laboratory Results: Coagulation
Listing 16.2.8.5A	Central Laboratory Results: Serum Complement
Listing 16.2.8.5B	Local Laboratory Results: Serum Complement
Listing 16.2.8.6	Local Laboratory Results: Cryoglobulins
Listing 16.2.8.7	Local Laboratory Results: Cold Agglutinins
Listing 16.2.8.8	Laboratory Results: Serology
Listing 16.2.8.9	Pregnancy Test Results

5.3.4. Vital Signs

The actual value and change from baseline to each on-study evaluation will be summarized for vital signs, including heart rate, blood pressure, respiratory rate, and temperature in degrees Celsius.

Vital sign measurements will be presented in a data listing.

Relevant Output:

Table 14.3.5.4	Summary and Change from Baseline for Vital Signs by Scheduled Visit and Dose Group (Safety Population)
Listing 16.2.9.1	Vital Signs

5.3.5. Physical Examination

All physical examination findings will be provided in a data listing.

Relevant Output:

Listing 16.2.9.2	Physical Examination Findings

5.3.6. Electrocardiogram

Actual ECG values and change from baseline will be summarized descriptively by scheduled visit, including heart rate and PR, QRS, QT, and QTcF (calculated by the Fridericia correction formula). QTcF will be calculated using the formula $QT/(RR^{1/3})$. If the RR interval is not collected, it will be calculated as 60 divided by the heart rate.

There will be a categorical summary of QTcF intervals, where the number and percent of patients experiencing a QTcF interval above the following limits between C1W1 and EOS will be summarized: >450, >480, and >500. Note that patients may be counted multiple times if applicable, for instance a patient with a maximum QTcF value of 520 would be counted in all 3 categories. Additionally, the number and percent of patients experiencing changes from baseline in the QTcF interval of >30 and >60 will be summarized.

QTcF intervals will also be summarized using the following categories: ≤450, 451-480, 481-500, >500 shift from baseline to each scheduled post-baseline value. A shift table will also be presented for heart rate using the following categories: <60 bpm, 60-100 bpm, and >100 bpm. The table will present shift from baseline to the greatest and smallest post baseline values using these categories.

Shift tables will be tabulated for individual and pooled dose groups using number and percentage of patients. ECG summaries by visit will use nominal visit and not include unscheduled values. Tables not summarized by visit will include all values, including unscheduled visits.

Electrocardiogram data will be provided in a data listing.

Relevant Output:

Table 14.3.5.5	Summary and Change from Baseline for Electrocardiogram Results by Scheduled Visit and Dose Group (Safety Population)
Table 14.3.5.6	Categorical Summary of QTcF Interval by Dose Group (Safety Population)

Table 14.3.5.7	Shifts in QTcF Interval from Baseline by Scheduled Visit and Dose Group (Safety Population)
Table 14.3.5.8	Shifts in Heart Rate Category from Baseline to Greatest and Lowest Post-Baseline Values by Dose Group (Safety Population)
Listing 16.2.9.4	12-Lead Electrocardiogram Interval and Overall Assessment

5.3.7. Concomitant Medications

Concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary Version Q12013 (or later). Results will be tabulated by anatomic therapeutic class (ATC) and preferred term.

Any medications that did not end prior to first dose will be classified as a concomitant medication, as well as medications that are ongoing or those missing the end date. In case of repeated occurrences per patient, a medication will only be counted once per ATC/preferred term.

The use of concomitant medications will be included in a by-patient data listing.

Relevant Output:

Table 14.3.5.9	Concomitant Medications (Safety Population)
Listing 16.2.9.5	Concomitant Medications

5.4. Efficacy Analyses

All efficacy analyses will be done using the Efficacy Evaluable (EE) Population, with select parameters repeated using the Safety Population as described in this section.

For patients who discontinue study treatment for any reason and start another treatment of their malignancy, all subsequent response assessments from the date of start of another treatment will be excluded from the analysis.

5.4.1. Primary Efficacy Analysis

The primary statistical analysis of efficacy will be performed on the investigator-assessed objective response rate (ORR), defined as the number of patients with a best response of MR, PR, VGPR, or CR divided by the number of patients in the EE Population. The ORR will be presented by dose level and overall with corresponding 90% confidence intervals (CIs) using the Wilson method. The CI will be computed using SAS; the software uses the following equation for computing the interval:

$$\frac{\hat{p} + \frac{z_{\alpha/2}^2}{2n} \pm z_{\alpha/2}\sqrt{(\hat{p}(1-\hat{p}) + z_{\alpha/2}^2/4n)/n}}{1 + z_{\alpha/2}^2/4n}$$

Relevant Output

Table 14.2.1.1	Objective Response Rate Primary Efficacy Analysis (Efficacy Evaluable Population)
Listing 16.2.6.1	Overall Disease Response

5.4.2. Secondary Efficacy Analyses

The following parameters will be analyzed by dose level and overall in both the EE and Safety Populations.

- Best overall response – The number and percentage of patients in each response category will be summarized.
- Percent and absolute change from baseline in quantitative serum levels of monoclonal and total IgM – Descriptive statistics, including change over time (i.e. percent change from baseline and absolute change from baseline) will be presented by dose group and overall for scheduled visits using central laboratory results. Only patients with a baseline value that is before the first dose of study treatment will be included in the change from baseline calculations. Local and central IgM values will be listed separately.

Relevant Output

Table 14.2.1.2A	Summary of Best Overall Response (Efficacy Evaluable Population)
Table 14.2.1.2B	Summary of Best Overall Response (Safety Population)
Table 14.2.2.1A	Percent Change from Baseline in Quantitative Serum Levels of Monoclonal and Total IgM by Scheduled Visit (Efficacy Evaluable Population)
Table 14.2.2.1B	Percent Change from Baseline in Quantitative Serum Levels of Monoclonal and Total IgM by Scheduled Visit (Safety Population)
Table 14.2.2.2A	Absolute Change from Baseline in Quantitative Serum Levels of Monoclonal and Total IgM by Scheduled Visit (Efficacy Evaluable Population)
Table 14.2.2.2B	Absolute Change from Baseline in Quantitative Serum Levels of Monoclonal and Total IgM by Scheduled Visit (Safety Population)
Listing 16.2.6.1	Overall Disease Response
Listing 16.2.6.2	Disease Response by Visit
Listing 16.2.6.3A	Disease Assessment – Part 1: Lymphadenopathy and Hepatomegaly
Listing 16.2.6.3B	Disease Assessment – Part 2: Splenomegaly
Listing 16.2.6.4	Immunoglobulin (IgM) Results
Listing 16.2.6.5A	Central Tumor Laboratory Assessments – Part 1: Electrophoresis and Protein Densitometry
Listing 16.2.6.5B	Central Tumor Laboratory Assessments – Part 2: Serum and Urine Assessments
Listing 16.2.6.6	Local Tumor Laboratory Assessments

5.4.3. Exploratory Analyses

The following investigational factors will be presented both globally across all cohorts and by dose level.

- Presence or absence of MyD88 L265P and CXCR4 mutations in tumor cells with regard to disease status– the summary of best overall response will be repeated by mutation status (present or absent) for both MyD88 L265P and CXCR4 mutations in the EE Population.
- Serum cytokine levels – Descriptive statistics, including absolute change from baseline will be presented by scheduled visit for all cytokines in the EE and Safety Populations. The median value at each scheduled visit (excluding EOT and EOS) will be plotted by treatment group with standard error bars.

- Hemoglobin and platelets – Descriptive statistics, including absolute change from baseline in hemoglobin and platelets will be presented for patients who have not been transfused during the course of the study by scheduled visit (excluding EOT and EOS) in the EE Population, using central laboratory results.

  Note: Patients with transfusion will be identified by concomitant medications with an ATC of "Blood and Related Products." For summary of hemoglobin, all patients with any medication where ATC = "Blood and Related Products," with the exception of the preferred term of "Platelets," will be excluded; for the platelet analysis, all patients with any medication where ATC = "Blood and Related Products" and preferred term of "Platelets" will be excluded.

- Immunogenicity and NF-κB results will be listed.

Additional exploratory analysis may occur. All efficacy data will be provided in data listings.

Relevant Output

Table 14.2.3.1	Exploratory Efficacy Analysis: Summary of Best Overall Response by MyD88 and CXCR4 Mutation Status (Efficacy Evaluable Population)
Table 14.2.4.1A	Summary of Actual Value and Absolute Change from Baseline in Serum Cytokine Levels by Scheduled Visit (Efficacy Evaluable Population)
Figure 14.2.4.1A	Median Serum Cytokine Levels by Dose Group and Scheduled Visit (Efficacy Evaluable Population)
Table 14.2.4.1B	Summary of Actual Value and Absolute Change from Baseline in Serum Cytokine Levels by Scheduled Visit (Safety Population)
Figure 14.2.4.1B	Median Serum Cytokine Levels by Dose Group and Scheduled Visit (Safety Population)
Table 14.2.4.2	Summary of Actual Value and Absolute Change from Baseline in Hemoglobin and Platelets in Patients Without Transfusions During the Study by Scheduled Visit (Efficacy Evaluable Population)
Listing 16.2.4.6	MyD88 L265P and CXCR4 Mutation Status
Listing 16.2.6.7	Central Efficacy Laboratory Assessments: Hemoglobin and Platelets
Listing 16.2.6.8	Central Efficacy Laboratory Assessments: Serum NF-κB
Listing 16.2.6.9	Immunogenicity Results: Anti-IMO-8400 Antibodies
Listing 16.2.6.10A	Serum Cytokines Test – Part 1
Listing 16.2.6.10B	Serum Cytokines Test – Part 2
Listing 16.2.6.10C	Serum Cytokines Test – Part 3
Listing 16.2.6.10D	Serum Cytokines Test – Part 4
Listing 16.2.6.11	Bone Marrow Biopsy Results

5.5. Pharmacokinetic Analyses

All plasma concentration data and parameter estimates will be described in a separate PK SAP and report.

6. CHANGES TO PLANNED ANALYSES

Protocol Section 12.2 describes a Safety/Intent-to-treat (ITT) Population and a Per-protocol (PP) Population for analysis. Section 2.1 of this document updates the title of the Safety/ITT Population to the Safety Population. The PP Population is not included in this document, and all efficacy analyses will be done on the EE Population, with select efficacy analyses also repeated on the Safety Population.

Protocol Section 12.5 describes the exploratory analysis of presence or absence of MyD88 L265P mutation in tumor cells. Section 2.2.5.2 of this document also includes an analysis of CXCR4 mutation.

Following an interim analysis to present the study results at the 2015 American Society of Hematology, the protocol was amended to explore two additional dose escalations since dose-limiting toxicity was not apparent. The last dosing cohort of 3.6 mg/kg/wk was never enrolled, however, as the Sponsor closed the trial prior to its scheduled opening. As a result, the efficacy objectives were reduced in scope substantially. Specifically, the following parameters and analyses described in Protocol Sections 12.4.1.2 and 12.5 are not included in this document:

- Secondary endpoints of time-to-progression, progression-free survival, and time to best observed response
- Secondary analysis of IgM data using a repeated measures mixed model
- Exploratory analyses of NF-κB inhibition and serum levels of antibody to IMO-8400 with regard to disease status

Regarding updates in safety parameters, Protocol Section 12.3 describes a time-to-event analysis for ISRs that is not included in this document.

7. REFERENCES

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Owen RG, Kyle RA, Stone MJ, et al. Response Assessment in Waldenström's Macroglobulinemia: update from the VIth International Workshop. Br J Haematology 2012; 160:171-176.

Treon SP, Xu L, Yang G, et al. MYD88 L265P somatic mutation in Waldenström's macroglobulinemia. N Engl J Med. 2012;367(9):826–833.

Young RM, **Staudt** LM. Targeting pathologic B cell receptor signaling in lymphoid malignancies. Nature Rev Drug Discovery. 2013; 12:229-243.

8. CLINICAL STUDY REPORT APPENDICES

8.1. List of Statistical Tables, Figures, and Listings to be Generated

8.2. Statistical Table and Figure Shells

The following statistical tables and figures will be produced.

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Table 14.0.1

Treatment Codes Applicable to Tables and Listings

Treatment Code	Treatment Description
0.6 mg/kg once weekly	IMO-8400 at 0.6 mg/kg once weekly dosing
1.2 mg/kg once weekly	IMO-8400 at 1.2 mg/kg once weekly dosing
1.2 mg/kg twice weekly	IMO-8400 at 1.2 mg/kg twice weekly dosing
2.4 mg/kg once weekly	IMO-8400 at 2.4 mg/kg once weekly dosing
3.6 mg/kg once weekly	IMO-8400 at 3.6 mg/kg once weekly dosing
Total	Pooled IMO-8400 dosing groups

Note: Dosing is based on body weight.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Only include dose groups that have at least 1 patient enrolled. Applicable to all tables.

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Table 14.1.1.1

Patient Enrollment and Disposition

Disposition	Sta-tistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Total Number of Patients Enrolled [1]	n	xx	xx	xx	xx	xx	xx
Study Populations							
Safety [2]	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Efficacy Evaluable (EE)[3]	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Discontinued Treatment	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Primary Reason for Treatment Discontinuation from EOT [4]							
DLT event	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Disease Progression	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Completion of 24 Weeks Treatment	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
AE, other than DLT	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Withdrawal of Consent	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Lost to Follow-Up	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Study Terminated by Sponsor	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Other	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Prematurely Discontinued Treatment [5]	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Primary Reason for Premature Treatment Discontinuation from EOS [6]							
Disease Progression	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
AE, related to study treatment	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
AE, unrelated to study treatment	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Non-compliance	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Lost to Follow-Up	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Physician Decision	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Study Terminated by Sponsor	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)

Note: AE = Adverse Event. DLT = Dose-Limiting Toxicity. EOT = End of Treatment. EOS = End of Study. Unless otherwise noted, percentage is based on total number of patients enrolled (treated).
[1] Enrolled: Patients who received at least one dose of study medication
[2] All patients who received at least one dose of the study treatment
[3] All patients who completed ≥1 cycle of therapy or those who discontinued due to progressive disease or DLT
[4] Percentages based on the number of patients who have discontinued treatment.
[5] Prematurely Discontinued Treatment: Patients who discontinued treatment prior to 24 weeks
[6] Percentage based on the number of patients who have prematurely discontinued treatment.
Reference Listings: 16.2.1.1, 16.2.3.1

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Table 14.1.2.1

Demographic Characteristics (Safety Population)

Parameter	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Age (years) [1]	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Ethnicity							
Hispanic/Latino	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Not Hispanic/Latino	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race							
American Indian or Alaska Native	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Asian	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Black	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Native Hawaiian or Other Pacific Islander	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
White	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Sex							
Male	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Female	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] Age calculated based on date of informed consent.
Reference Listing: 16.2.4.1

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Table 14.1.2.2

Baseline Characteristics (Safety Population)

Parameter	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Baseline Height (cm)	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	(xx.xx)	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Baseline Weight (kg)	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	(xx.xx)	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Baseline BMI (kg/m^2) [1]	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	(xx.xx)	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Baseline ECOG Performance Status [2]							
0	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MyD88 Mutation Status							
Present	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Absent	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CXCR4 Mutation Status							
Present	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Absent	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] Body Mass Index = Weight (kg)/(Height (m))^2.
[2] ECOG = Eastern Cooperative Oncology Group. 0 = Fully active, able to carry on all pre-disease performance without restriction. 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature. 2 = Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours. 3 = Capable of only limited self-care; confined to bed or chair more than 50% of waking hours. 4 = Completely disabled.
Reference Listings: 16.2.4.3, 16.2.4.6, 16.2.9.1, 16.2.9.3

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Programming note: Include rows for Unknown and Missing for mutation status if needed.

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Table 14.1.3.1

Disease History and Baseline Disease Characteristics (Safety Population)

Parameter	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Time Since WM Diagnosis (yrs) [1]	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min,Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Baseline IPSSWM							
Low	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Intermediate	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
High	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Baseline Total IgM (mg/dL)	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min,Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Baseline Monoclonal IgM (g/dL)	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min,Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Baseline Hemoglobin (g/dL)	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min,Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Baseline Platelet Count (K/cu mm)	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min,Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Baseline Beta-2 Microglobulin (mg/dL)	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min,Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Note: IPSSWM = International Prognostic Scoring System for WM. Central laboratory results are presented.
[1] Time from WM diagnosis to date of first dose of study drug.
Reference Listings: 16.2.4.3, 16.2.6.5A, 16.2.6.5B, 16.2.6.6

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Programming note: Verify units for the laboratory parameters. Use central results for laboratory parameters. See SAP Section 4.10 for handing of missing/partial dates for calculation of time since diagnosis.

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Table 14.1.4.1

Prior Treatments (Safety Population)

Parameter	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Received at Least 1 Prior Therapy	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Agent/Treatment [1]							
Rituximab	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Bortezomib	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Cyclophosphamide	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Dexamethasone	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Vincristine	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Prednisone	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Fludarabine	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Cladribine	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Experimental [2]	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Ibrutinib	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Leukeran	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Best Overall Response [3]							
Complete Response (CR)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Very Good Partial Response (VGPR)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Partial Response (PR)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Minor Response (MR)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Stable Disease (SD)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Progressive Disease (PD)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Not Evaluable	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Delayed Response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: AE = Adverse Event
[1] Agent/Treatment categorized by clinical review. Only select treatments are summarized.
[2] Experimental treatments include KPT-330 and AVILA 292.
[3] Percentages based on number that received at least 1 prior therapy.
[4] Time from end of prior therapy to date of first dose of IMO-8400.
Reference Listing: 16.2.4.4
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Programming note: See page 2.

Table 14.1.4.1

Prior Treatments (Safety Population

Parameter	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Reason for Discontinuation [3]							
Failure to respond	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Treatment related AE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Not treatment related AE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patient Non-Compliance	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Physician Decision	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Unknown	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Prior Therapies	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min,Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Number of Prior Therapies Categories							
1 Prior Therapy	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
2 Prior Therapies	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
3 Prior Therapies	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
4+ Prior Therapies	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Days Since Most Recent Prior Therapy [4]	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min,Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Note: AE = Adverse Event
[1] Agent/Treatment categorized by clinical review. Only select treatments are summarized.
[2] Experimental treatments include KPT-330, AVILA 292, and TRU-16.
[3] Percentages based on number that received at least 1 prior therapy.
[4] Time from end of prior therapy to date of first dose of IMO-8400.
Reference Listing: 16.2.4.4

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Programming note: Number of days since Most Recent Prior Therapy = (date of first dose – end date of most recent prior therapy)
Update the experimental treatments in the footnote to include all experimental treatments at the time of the analysis. See SAP Section 4.10 for handing of missing/partial dates.

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Table 14.1.5.1

Baseline Waldenström's Macroglobulinemia Symptoms (Safety Population)

Baseline Symptom	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Bleeding Events	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Fatigue	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Anemia	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Thrombocytopenia	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Leukemia/Neutropenia	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Fever	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Hyperviscosity	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Neuropathy	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lymphadenopathy	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Weight Loss	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Headache	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Night Sweats	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Vision Changes	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Reference Listing: 16.2.4.5

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Table 14.2.1.1

Objective Response Rate Primary Efficacy Analysis (Efficacy Evaluable Population)

Parameter	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Objective Response Rate (CR/VGPR/PR/MR)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	90%CI [1]	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx	x.xxx,x.xxx

Note: CR = Complete response. VGPR = Very good partial response. PR = Partial response. MR = Minor response.
[1] CI = Confidence interval. Confidence intervals calculated using Wilson's method.
Reference Listing: 16.2.6.1

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Table 14.2.1.2A

Summary of Best Overall Response (Efficacy Evaluable Population)

Parameter	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Best Overall Response							
Complete response (CR)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Very good partial response (VGPR)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Partial response (PR)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Minor response (MR)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Stable disease (SD)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Progressive disease (PD)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Not evaluable	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Delayed response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Reference Listing: 16.2.6.1

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Repeat for:
Table 14.2.1.2B Summary of Best Overall Response (Safety Population)

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Table 14.2.2.1A

Percent Change from Baseline in Quantitative Serum Levels of Monoclonal and Total IgM by Scheduled Visit (Efficacy Evaluable Population)

Parameter: [Describe: Monoclonal IgM (g/dL)]

Visit	Statistic	Value	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Baseline	n	Actual Value	xx	xx	xx	xx	xx	xx
	Mean (SD)		xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
C1W9	n	Actual Value	xx	xx	xx	xx	xx	xx
	Mean (SD)		xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	n	Percent Change from Baseline	xx	xx	xx	xx	xx	xx
	Mean (SD)		xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Etc.								

Note: Baseline = the most recent laboratory assessment before the first dose of study medication.
Reference Listing: 16.2.6.4

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Present Total IgM or Monoclonal IgM as the parameter, with the unit, using central lab results only.

Repeat for:
Table 14.2.2.1B Percent Change from Baseline in Quantitative Serum Levels of Monoclonal and Total IgM by Scheduled Visit (Safety Population)

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Table 14.2.2.2A

Absolute Change from Baseline in Quantitative Serum Levels of Monoclonal and Total IgM by Scheduled Visit (Efficacy Evaluable Population)

Parameter: [Monoclonal IgM (g/dL)]

Visit	Statistic	Value	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Baseline	n	Actual	xx	xx	xx	xx	xx	xx
	Mean (SD)	Value	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		(xx.xx)	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
C1W9	n	Actual	xx	xx	xx	xx	xx	xx
	Mean (SD)	Value	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		(xx.xx)	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	n	Change	xx	xx	xx	xx	xx	xx
	Mean (SD)	from	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	Baseline	(xx.xx)	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Etc.								

Note: Baseline = the most recent laboratory assessment before the first dose of study medication.
Reference Listing: 16.2.6.4

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Present Total IgM or Monoclonal IgM as the parameter, with the unit, using central lab results only.

Repeat for:
Table 14.2.2.2B Absolute Change from Baseline in Quantitative Serum Levels of Monoclonal and Total IgM by Scheduled Visit (Safety Population)

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Table 14.2.3.1

Exploratory Efficacy Analysis: Summary of Best Overall Response by MyD88 and CXCR4 Mutation Status (Efficacy Evaluable Population)

Mutation Status	Best Overall Response	Sta-tistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
MyD88								
Present	Complete response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Very good partial response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Partial response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Minor response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Stable disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Progressive disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Not evaluable	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Delayed response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Absent	Complete response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Very good partial response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Partial response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Minor response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Stable disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Progressive disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Not evaluable	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Delayed response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CXCR4								
Present	Complete response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Very good partial response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Partial response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Minor response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Stable disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Progressive disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Not evaluable	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Delayed response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Absent	Complete response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Very good partial response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Partial response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Minor response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Stable disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Progressive disease	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Not evaluable	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Delayed response	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Reference Listings: 16.2.4.6, 16.2.6.1

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Table 14.2.4.1A

Summary of Actual Value and Absolute Change from Baseline in Serum Cytokine Levels by Scheduled Visit (Efficacy Evaluable Population)

Parameter: [Cytokine 1 (unit)]

Visit	Statistic	Value	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Baseline	n	Actual	xx	xx	xx	xx	xx	xx
	Mean (SD)	Value	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
C1W9	n	Actual	xx	xx	xx	xx	xx	xx
	Mean (SD)	Value	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	n	Change	xx	xx	xx	xx	xx	xx
	Mean (SD)	from	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	Baseline	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Etc.								

Note: Baseline = the most recent laboratory assessment before the first dose of study medication.
Reference Listings: 16.2.6.10A, 16.2.6.10B, 16.2.6.10C, 16.2.6.10D

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: For the figures, present the median value for each treatment group at each visit (excluding EOT and EOS), and include standard error bars.

Figure:
Figure 14.2.4.1A Median Serum Cytokine Levels by Dose Group and Scheduled Visit (Efficacy Evaluable Population)

Repeat for:
Table 14.2.4.1B Summary of Actual Value and Absolute Change from Baseline in Serum Cytokine Levels by Scheduled Visit (Safety Population)
Figure 14.2.4.1B Median Serum Cytokine Levels by Dose Group and Scheduled Visit (Safety Population)

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Table 14.2.4.2

Summary of Actual Value and Absolute Change from Baseline in Hemoglobin and Platelets in Patients Without Transfusions During the Study by Scheduled Visit (Efficacy Evaluable Population)

Parameter: [Parameter (unit)]

Visit	Statistic	Value	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Baseline	n	Actual	xx	xx	xx	xx	xx	xx
	Mean (SD)	Value	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
C1W9	n	Actual	xx	xx	xx	xx	xx	xx
	Mean (SD)	Value	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	n	Change	xx	xx	xx	xx	xx	xx
	Mean (SD)	from	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	Baseline	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x

Etc.

Note: Baseline = the most recent laboratory assessment before the first dose of study medication.
Reference Listing: 16.2.6.6

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Programming note: Use central labs only.

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Table 14.3.1.1

Summary of Treatment-Emergent Adverse Events (Safety Population)

Parameter	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
At Least 1 TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least 1 Related TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least 1 Grade >=3 TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least 1 SAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least 1 DLT	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least 1 TEAE Leading to Death	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least 1 TEAE Leading to Premature Treatment Discontinuation	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: TEAE = Treatment-Emergent Adverse Event. SAE = Serious Adverse Event. DLT = Dose Limiting Toxicity.
Related = Adverse events identified by the Investigator as probably or possibly related to the study drug, or with a missing relationship.
Reference Listing: 16.2.7.1

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Table 14.3.1.2

Incidence of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term (Safety Population)

MedDRA System Organ Class / Preferred Term	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
At Least 1 TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.							

Note: TEAE = Treatment-Emergent Adverse Event. Adverse Events coded per MedDRA Version 16.1. If a patient experienced more than one episode of an adverse event, that patient is counted once within a System Organ Class and Preferred Term.
Reference Listing: 16.2.7.1

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Table 14.3.1.3

Incidence of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term and Strongest Relationship to Study Drug (Safety Population)

MedDRA System Organ Class/ Preferred Term	Relation-ship	Sta-tistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
At Least 1 TEAE	Related	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
	Not-Related	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
SOC 1	Related	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
	Not-Related	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Preferred Term 1	Related	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
	Not-Related	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Preferred Term 2	Related	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
	Not-Related	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Etc.								
Etc.								

Note: TEAE = Treatment-Emergent Adverse Event. Adverse Events coded per MedDRA Version 16.1.
Drug related adverse events are those which are identified by the investigator as probably or possibly related to the study drug, or with a missing relationship, and not related adverse events are those which are unlikely and not related to the study drug. If a patient experienced more than one episode of an adverse event, that patient is counted once within a System Organ Class and Preferred Term by the strongest relationship to study drug.
Reference Listing: 16.2.7.1

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Table 14.3.1.4

Incidence of Non-Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
At Least 1 Non-serious TEAE	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
SOC 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.							

Note: TEAE = Treatment-Emergent Adverse Event. Adverse Events coded per MedDRA Version 16.1. If a patient experienced more than one episode of an adverse event, that patient is counted once within a System Organ Class and Preferred Term.
Reference Listing: 16.2.7.1

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Table 14.3.1.5

Incidence of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
At Least 1 Serious TEAE	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
SOC 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.							

Note: TEAE = Treatment-Emergent Adverse Event. Adverse Events coded per MedDRA Version 16.1. If a patient experienced more than one episode of an adverse event, that patient is counted once within a System Organ Class and Preferred Term.
Reference Listing: 16.2.7.1

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

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Table 14.3.1.6

Incidence of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term and by Highest Grade
(Safety Population)

MedDRA System Organ Class Preferred Term	Sta- tistic	0.6 mg/kg once weekly (N=xx) Grade 1 or 2	 Grade 3	 Grade >= 4	 Total	1.2 mg/kg once weekly (N=xx) Grade 1 or 2	 Grade 3	 Grade >= 4	 Total
At Least 1 TEAE	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
SOC 1	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Preferred Term 1	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Preferred Term 2	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Etc.	n (%)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Etc.									

Note: TEAE = Treatment-Emergent Adverse Event. Adverse Events coded per MedDRA Version 16.1. If a patient experienced more than one episode of an adverse event, that patient is counted once within a System Organ Class and Preferred Term by the highest severity.
Reference Listing: 16.2.7.1

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Move onto multiple pages as needed; include all dose groups with at least one patient and total (0.6 once weekly, 1.2 once weekly, 1.2 twice weekly, 2.4 once weekly, 3.6 once weekly, and total).

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Table 14.3.1.7

Incidence of Dose-Limiting Toxicity Adverse Events by MedDRA System Organ Class and Preferred Term (Safety Population)

MedDRA System Organ Class Preferred Term	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
At Least 1 DLT	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: DLT = Dose-Limiting Toxicity. Adverse Events coded per MedDRA Version 16.1. If a patient experienced more than one episode of an adverse event, that patient is counted once within a System Organ Class and Preferred Term.
Reference Listing: 16.2.7.1

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Table 14.3.1.8

Incidence of Observed Local Injection Site Reactions by Worst Grade Post-Baseline (Safety Population)

Symptom / Toxicity Grade	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Pain							
Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Tenderness							
Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
<Repeat above format for Pruritus and Induration>							
Blister							
Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Blister (mm)	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	25th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	75th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	90th Percentile	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
<Repeat above format (2 rows each) for Ulceration, Erythema, and Necrosis>							

Note: In the case of multiple grades, only the worst grade post baseline is counted for each patient and symptom regardless of the site of injection.
Reference Listing: 16.2.7.6

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Include higher grades if there are any to report for each symptom.

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Table 14.3.1.9

Incidence of Observed Local Injection Site Reactions by Worst Grade and Scheduled Visit (Safety Population)

Visit	Symptom / Toxicity Grade	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Day 1	Pain							
	Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 5	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Tenderness							
	Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 5	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.							
Day 3	Pain							
	Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 5	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Tenderness							
	Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Grade 5	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.							
Etc.								

Note: In the case of multiple grades, only the worst grade at each visit is counted for each patient and symptom regardless of the site of injection.
Reference Listing: 16.2.7.6

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Include all symptoms and all visits.

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Table 14.3.2.1

Listing of Adverse Events Leading to Death

Dose Group:

			Onset		End									
Patient Number	SOC [1]	Preferred Term	Date/ Time	Rel Day [2]	Date/ Time	Rel Day [2]	Sever- ity [3]	SAE	TEAE	DLT	Rela- tionship [4]	Action Taken with IMO-8400	Action Taken for AE	Sequelae at Resolution
								Yes No	Yes No	Yes No				Yes: No

Note: SOC = System Organ Class. SAE = Serious adverse event. TEAE = Treatment-emergent adverse event. DLT = Dose limiting toxicity. CM = Concomitant medication. Adverse events coded per MedDRA version 16.1.
[1] Refer to listing 16.0.1 for the full SOC name associated with the corresponding abbreviation.
[2] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[3] 1 = Grade 1: Mild. 2 = Grade 2: Moderate. 3 = Grade 3: Marked. 4 = Grade 4: Extreme. 5 = Grade 5: Death.
[4] Relationship to Study Drug: Prob Rel = Probably Related, Poss Rel = Possibly Related, Unlike Rel = Unlikely Related, Not Rel = Not related.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If sequelae at resolution, concatenate specifics (Yes: Specify sequelae).

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Table 14.3.2.2

Listing of Serious Adverse Events

Dose Group:

Patient Number	SOC [1]	Preferred Term	Onset Date/ Time	Onset Rel Day [2]	End Date/ Time	End Rel Day [2]	Sever-ity [3]	TEAE	DLT	Rela-tionship [4]	Action Taken with IMO-8400	Action Taken for AE	Sequelae at Resolution
								Yes No	Yes No				Yes: No

Note: SOC = System Organ Class. SAE = Serious adverse event. TEAE = Treatment-emergent adverse event. DLT = Dose limiting toxicity. CM = Concomitant medication. Adverse events coded per MedDRA version 16.1.
[1] Refer to listing 16.0.1 for the full SOC name associated with the corresponding abbreviation.
[2] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[3] 1 = Grade 1: Mild. 2 = Grade 2: Moderate. 3 = Grade 3: Marked. 4 = Grade 4: Extreme. 5 = Grade 5: Death.
[4] Relationship to Study Drug: Prob Rel = Probably Related, Poss Rel = Possibly Related, Unlike Rel = Unlikely Related, Not Rel = Not related.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

DATE: DDMMMYYYY HH:MM

Programming note: If sequelae at resolution, concatenate specifics (Yes: Specify sequelae).

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Table 14.3.2.3

Listing of Dose Limiting Toxicities

Dose Group:

			Onset		End								
Patient Number	SOC [1]	Preferred Term	Date/ Time	Rel Day [2]	Date/ Time	Rel Day [2]	Severity [3]	SAE	TEAE	Relationship [4]	Action Taken with IMO-8400	Action Taken for AE	Sequelae at Resolution
								Yes	Yes				Yes:
								No	No				No

Note: SOC = System Organ Class. SAE = Serious adverse event. TEAE = Treatment-emergent adverse event. DLT = Dose limiting toxicity. CM = Concomitant medication. Adverse events coded per MedDRA version 16.1.
[1] Refer to listing 16.0.1 for the full SOC name associated with the corresponding abbreviation.
[2] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[3] 1 = Grade 1: Mild. 2 = Grade 2: Moderate. 3 = Grade 3: Marked. 4 = Grade 4: Extreme. 5 = Grade 5: Death.
[4] Relationship to Study Drug: Prob Rel = Probably Related, Poss Rel = Possibly Related, Unlike Rel = Unlikely Related, Not Rel = Not related.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If sequelae at resolution, concatenate specifics (Yes: Specify sequelae).

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Table 14.3.2.4

Listing of Premature Treatment Discontinuations Due to Adverse Events

Dose Group:

			Onset		End									
Patient Number	SOC [1]	Preferred Term	Date/ Time	Rel Day [2]	Date/ Time	Rel Day [2]	Severity [3]	SAE	TEAE	DLT	Relationship [4]	Action Taken with IMO-8400	Action Taken for AE	Sequelae at Resolution
								Yes	Yes	Yes				Yes:
								No	No	No				No

Note: SOC = System Organ Class. SAE = Serious adverse event. TEAE = Treatment-emergent adverse event. DLT = Dose limiting toxicity. CM = Concomitant medication. Adverse events coded per MedDRA version 16.1.
[1] Refer to listing 16.0.1 for the full SOC name associated with the corresponding abbreviation.
[2] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[3] 1 = Grade 1: Mild. 2 = Grade 2: Moderate. 3 = Grade 3: Marked. 4 = Grade 4: Extreme. 5 = Grade 5: Death.
[4] Relationship to Study Drug: Prob Rel = Probably Related, Poss Rel = Possibly Related, Unlike Rel = Unlikely Related, Not Rel = Not related.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If sequelae at resolution, concatenate specifics (Yes: Specify sequelae).

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Table 14.3.5.1

Study Drug Exposure (Safety Population)

Parameter	Statistics	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Cumulative Exposure (mg) [1]	n	xx	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Cycles Received [2]							
Received <1 Cycle	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Received 1 Cycle	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Received 2 Cycles	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Received 3 Cycles	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Received 4 Cycles	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Doses Received	n	xx	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Number of Missed Doses	n	xx	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Reason Dose Missed [3]							
DLT	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
AE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Visit missed	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
DME	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: AE = Adverse event. DLT = Dose limiting toxicity. DME = Dose modifying event.
[1] Cumulative exposure is the sum of all doses received, where each dose is calculated as [assigned dose (mg/kg) * volume administered (mL)] / concentration of 0.007 (mL/kg).
[2] A completed cycle is defined as having received 8 weeks of treatment for that cycle.
[3] Percentages based on number of patients that had at least one missed dose. Each patient is tallied once per reason, regardless of how many doses were missed for that reason.
Reference Listing: 16.2.5.1

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Add “unknown” as a reason dose missed if applicable. Add more cycles if needed for cycles received.

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Table 14.3.5.2A

Summary and Change from Baseline for Hematology Parameters by Scheduled Visit and Dose Group (Safety Population)

Parameter: [Lab Test 1 (unit)]

Visit	Statistic	Value	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Baseline	n	Actual Value	xx	xx	xx	xx	xx	xx
	Mean (SD)		xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
C1W9	n	Actual Value	xx	xx	xx	xx	xx	xx
	Mean (SD)		xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	n	Change from Baseline	xx	xx	xx	xx	xx	xx
	Mean (SD)		xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Etc.								

Note: Baseline = the most recent laboratory assessment before the first dose of study medication.
Reference Listings: 16.2.8.1A, 16.2.8.1B

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Repeat for:
Table 14.3.5.2B Summary and Change from Baseline for Chemistry Parameters by Scheduled Visit and Dose Group (Safety Population)
Table 14.3.5.2C Summary and Change from Baseline for Coagulation Parameters by Scheduled Visit and Dose Group (Safety Population)
Table 14.3.5.2D Summary and Change from Baseline for Serum Complement Parameters by Scheduled Visit and Dose Group (Safety Population)

Programming note: Use central labs only. Update references listings for the repeat tables.

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Table 14.3.5.3A

Shifts from Baseline to Worst CTCAE Grade Post-Baseline in Hematology Parameters by Dose Group (Safety Population)

Laboratory Parameter	Dose Group	Baseline Results	Statistic	Worst CTC Grade Post-Baseline Results: WNL	Grade 1	Grade 2	Grade 3	Grade 4	Missing
Lab Test 1 (unit)	0.6 mg/kg once weekly (N=xx)	WNL	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Missing	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1.2 mg/kg once weekly (N=xx)	WNL	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Missing	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.								
Lab Test 2 (unit)	0.6 mg/kg once weekly (N=xx)	WNL	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Grade 4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Missing	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.								
Etc.									

Note: Baseline = the most recent laboratory assessment before the first dose of study medication. WNL = Within Normal Limit.
Reference Listing: 16.2.8.1A, 16.2.8.1B

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note: Repeat analyses for all laboratory parameters and all visits. Include all dose groups that have at least 1 patient and total (0.6 once weekly, 1.2 once weekly, 1.2 twice weekly, 2.4 once weekly, 3.6 once weekly, and total).

Repeat for:
Table 14.3.5.3B Shifts from Baseline to Worst CTCAE Grade Post-Baseline in Chemistry Parameters by Dose Group (Safety Population)
Table 14.3.5.3C Shifts from Baseline to Worst CTCAE Grade Post-Baseline in Coagulation Parameters by Dose Group (Safety Population)

Programming note: Use central labs only. Update references listings for the repeat tables.

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Table 14.3.5.4

Summary and Change from Baseline for Vital Signs by Scheduled Visit and Dose Group (Safety Population)

Parameter: [VS 1 (unit)]

Visit	Statistic	Value	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Baseline	n	Actual Value	xx	xx	xx	xx	xx	xx
	Mean (SD)		xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
C1W9	n	Actual Value	xx	xx	xx	xx	xx	xx
	Mean (SD)		xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	n	Change from	xx	xx	xx	xx	xx	xx
	Mean (SD)	Baseline	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Etc.								

Reference Listing: 16.2.9.1

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note: Repeat analyses for all vital sign parameters.

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Table 14.3.5.5

Summary and Change from Baseline for Electrocardiogram Results by Scheduled Visit and Dose Group (Safety Population)

Parameter: [ECG 1 (unit)]

Visit	Statistic	Value	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Baseline	n	Actual Value	xx	xx	xx	xx	xx	xx
	Mean (SD)		xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
C1W9	n	Actual Value	xx	xx	xx	xx	xx	xx
	Mean (SD)		xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
	n	Change from Baseline	xx	xx	xx	xx	xx	xx
	Mean (SD)		xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median		xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min,Max		xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x	xx.x,xx.x
Etc.								

Reference Listing: 16.2.9.4

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming note: Repeat for all ECG parameters; use derived QTcF for the QTc interval.

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Table 14.3.5.6

Categorical Summary of QTcF Interval by Dose Group (Safety Population)

QTcF Observation	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Subjects who experienced a QTcF:							
>450	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
>480	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
>500	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects who experienced change from baseline in QTcF of:							
>30	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
>60	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Reference Listing: 16.2.9.4

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Programming Note: Subjects may be counted in multiple categories.

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Table 14.3.5.7

Shifts in QTcF Interval from Baseline by Scheduled Visit and Dose Group (Safety Population)

				Post-Baseline Value				
Visit	Dose Group	Baseline Results	Statistic	<=450	451-480	481-500	>500	Missing
C1W2	0.6 mg/kg once weekly (N=xx)	<=450	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		451-480	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		481-500	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		>500	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Missing	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Etc.							

Note: Baseline = the most recent assessment before the first dose of study medication. QTc calculated using Fridericia correction formula.
Reference Listing: 16.2.9.4

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note: Include all dose groups that have at least 1 patient and total (0.6 once weekly, 1.2 once weekly, 1.2 twice weekly, 2.4 once weekly, 3.6 once weekly, and total).

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Table 14.3.5.8

Shifts in Heart Rate Category from Baseline to Greatest and Lowest Post-Baseline Values by Dose Group (Safety Population)

			Greatest Post-Baseline Value				Lowest Post-Baseline Value			
Dose Group	Baseline Results	Statistic	<60 bpm	60-100 bpm	>100 bpm	Missing	<60 bpm	60-100 bpm	>100 bpm	Missing
0.6 mg/kg once weekly (N=xx)	<60 bpm	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	60-100 bpm	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	>100 bpm	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Missing	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
1.2 mg/kg once weekly (N=xx)	<60 bpm	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	60-100 bpm	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	>100 bpm	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Missing	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.										

Note: Baseline = the most recent assessment before the first dose of study medication.
Reference Listing: 16.2.9.4

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note: Include all dose groups and total (0.6 once weekly, 1.2 once weekly, 1.2 twice weekly, 2.4 once weekly, 3.6 once weekly, and total).

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Table 14.3.5.9

Concomitant Medications (Safety Population)

ATC Classification	Statistic	0.6 mg/kg once weekly (N=xx)	1.2 mg/kg once weekly (N=xx)	1.2 mg/kg twice weekly (N=xx)	2.4 mg/kg once weekly (N=xx)	3.6 mg/kg once weekly (N=xx)	Total (N=xx)
Any Concomitant Medication	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CM CLASS 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CM Code 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CM Code 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CM CLASS 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CM Code 1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CM Code 2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.							

[1] ATC = Anatomic Therapeutic Classification from WHO Drug Dictionary Q12013.
Reference Listing: 16.2.9.5

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: HH:MM/DDMMMYYYY

Programming Note: Repeat analyses for all CM classes and CM codes. Update drug dictionary if necessary at time of programming.

8.3. Data Listing Shells

The following data listings will be produced.

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Listing 16.0.1

System Organ Class Abbreviations

SOC	Abbreviations
Blood and lymphatic system disorders	BLOOD
Cardiac disorders	CARD
Congenital, familial and genetic disorders	CONGN
Ear and labyrinth disorders	EAR
Endocrine disorders	ENDO
Eye disorders	EYE
Gastrointestinal disorders	GASTR
General disorders and administration site conditions	GENRL
Hepatobiliary disorders	HEPAT
Immune system disorders	IMMUN
Infections and infestations	INFCT
Injury, poisoning and procedural complications	INJUR
Investigations	INVST
Metabolism and nutrition disorders	METAB
Musculoskeletal and connective tissue disorders	MUSCL
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	NEOPL
Nervous system disorders	NERV
Pregnancy, puerperium and perinatal conditions	PREG
Psychiatric disorders	PSYCH
Renal and urinary disorders	RENAL
Reproductive system and breast disorders	REPRO
Respiratory, thoracic and mediastinal disorders	RESP
Skin and subcutaneous tissue disorders	SKIN
Social circumstances	SOCL
Surgical and medical procedures	SURG
Vascular disorders	VASC

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: Verify the list of abbreviations includes all SOCs.

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Listing 16.2.1.1

Patient Disposition

Dose Group	Patient Number	Number of Cycles Received [1]	Patient Had a Dose Level Reduction	Date of Last Dose	Rel Day [2]	Primary Reason for Termination of Treatment	Reason Discontinued Study	Reason End of Study Visit Not Completed
			Y:					
			N					

[1] A completed cycle is defined as having received 8 weeks of treatment for that cycle; 0 indicates patient completed < 1 cycle.
[2] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: Reason discontinued taken from “Please indicate the primary reason patient did not complete all weeks” question. If the patient had a dose level reduction, concatenate the reduced dose level “Y: “.

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Listing 16.2.1.2

End of Treatment (EOT) Visit Status

Dose Group	Patient Number	Date of Treatment Termination	Rel Day [1]	Primary Reason for Termination of Treatment	Specifics	Comments	Patient Had a Dose Level Reduction	Date of EOT visit	Rel Day [1]
				DLT event			Y:		
				Disease Progression			N		
				Completion of 24 weeks treatment					
				AE					
				Withdrawal of Consent					
				Lost to Follow-Up					
				Study Termination by Sponsor					
				Other					

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: Primary reason for termination of treatment taken from the EOT page. Include additional specification under "Specifics". Include "Please specify DLT event", "Please specify disease progression", "Please specify other adverse event", "Please explain all attempts to contact the patient", and "Please specify other". If the patient had a dose level reduction, concatenate the reduced dose level "Y: ".

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Listing 16.2.1.3

End of Study (EOS) Visit Status

Dose Group	Patient Number	Date of Visit/ Rel Day [1]	Reason Visit Not Completed	Date of Death/ Rel Day [1]	Cause of Death	Date Last Seen/ Rel Day [1]	Completed 24 Weeks of Study Treatment	Primary Reason Patient did not Complete 24 Weeks	Comments
			Death				Yes	Disease Progression	
			Lost to Follow-up				No	AE related to study treatment	
			Withdrawal of Consent					AE not related to study treatment	
			Patient enrolled in 8400-404					Pregnancy	
								Lost to Follow-up	
								Withdrawal of Consent	
								Physician Decision	
								Study terminated by Sponsor	

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

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Listing 16.2.2.1

Listing of Inclusion/Exclusion Criteria Not Met

Dose Group	Patient Number	IN/EX Criteria Not Met	Waiver Granted	Waiver Details	Comments
			Yes		
			No		

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

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Listing 16.2.2.2

Protocol Deviations

Dose Group	Patient Number	Date of Deviation	Rel Day [1]	Category of Deviation	Deviation Specifics	Comments
				Inclusion / Exclusion Criteria Not Met		
				Prohibited Medication Taken		
				Blood Specimen Collection Missed/ Out of Window		
				Other Protocol Procedure Missed/ Out of Window		
				IMO-8400 Dose Missed		
				Other		

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

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Listing 16.2.3.1

Study Populations

Dose Group	Patient Number	Safety Population	Efficacy Evaluable Population	Reason Excluded from the Efficacy Evaluable Population

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.4.1

Demographic Characteristics

Dose Group	Patient Number	Informed Consent Date	Protocol Version Date	Date of Birth	Age (Years)	Sex	Of Child-bearing Potential	Race	Ethnicity
						Male	Yes	American Indian or Alaska Native	Hispanic or Latino
						Female	No	Asian	Not Hispanic or Latino
								Black	
								Native Hawaiian or Other Pacific Islander	
								White	
								Other:	

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: Concatenate specifics if “other” is chosen for race (Other: Specify).

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Listing 16.2.4.2

Medical History

Dose Group	Patient Number	System	Disease/ Procedure	Start Date	End Date	Ongoing at Screening
						Yes
						No

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

DATE: HH:MM/DDMMMYYYY

Programming note: if Ongoing = Yes, mark ONGOING in end date column.

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Listing 16.2.4.3

Waldenström's Macroglobulinemia Disease History

						Hospitalized in the Past Year			Treatment-related AEs in Past 3 Months			
Dose Group	Patient Number	Date of Diagnosis	Date of First Treatment for WM	Disease Status [1]	IPSSWM [2]	Y/N	Date of Discharge	Discharge Diagnosis	Y/N	Event Term	Start Date	End Date
				Refrac Relap Unk	Low Inter High	Yes No			Yes No			

Note: AE = Adverse Event
[1] Refrac = Refractory. Relap = Relapsed. Unk = Unknown.
[2] IPSSWM = International Prognostic Scoring System for WM. Inter = Intermediate.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

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Listing 16.2.4.4

Prior Waldenström's Macroglobulinemia Therapy

Dose Group	Patient Number	Agent/ Treatment	Other Treatment	Agent/Treatment Categorized [1]	Start Date	Stop Date	Best Clinical Response	Reason for Discontinuation	AEs experienced with this treatment	Total Number of Prior Treatment Regimens

Note: AE = Adverse Event.
[1] Agent/Treatment categorized by clinical review.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If there was a combination of treatments recorded in eCRF and some of the drug names were categorized, please present it here as combination but with updated drug name. For example for pt 506-101 if 'Ritux/Bendamustin' was used, then 'Agent/Treatment' column will state 'Other', 'Other Treatment' will state 'Ritux/Bendamustin' and Agent/Treatment Categorized' will be 'Rituximab/Bendamustin'.

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Listing 16.2.4.5

Baseline Waldenström's Macroglobulinemia Symptoms

Dose Group	Patient Number	Symptoms Present at Baseline	Date of Occurrence	Severity	Clinically Significant
		Bleeding Events		Grade 1: Mild	Yes
		Fatigue		Grade 2: Moderate	No
		Anemia		Grade 3: Marked	
		Thrombocytopenia		Grade 4: Extreme	
		Leukemia / neutropenia			
		Fever			
		Hyperviscosity			
		Neuropathy			
		Lymphadenopathy			
		Weight loss			
		Headache			
		Night Sweats			
		Vision Changes			
		Other:			

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Programming note: Concatenate specifics if "other" is chosen as a sign/symptom (Other: Specify).

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Listing 16.2.4.6

MyD88 L265P and CXCR4 Mutation Status

Dose Group	Patient Number	Date of Assessment	Rel Day [1]	Mutation	Mutation Status
				MyD88 L265P	Present
				CXCR4	Absent

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.5.1

Study Drug Exposure

Dose Group: [Describe] Patient Number	Cycle/ Week	Both Doses Administered	Injection	Location	Date/ Time	Rel Day [1]	Site of Injection [2]	Volume Dispensed (mL)	Dose (mg) [3]	Entire Dose Administered	Reason Dose Missed [4]	Cumulative Exposure (mg) [5]
		Yes	1	Site						Yes	AE-Rel	
		No: Only 1	2	Home Visit						No: [Specify]	AE-NR	
		No: Neither									Missed Visit	
											Other: [Specify]	

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] RUQ= Right Upper Quadrant, LUQ= Left Upper Quadrant, RLQ= Right Lower Quadrant, LLQ= Left Lower Quadrant.
[3] Calculated as [assigned dose (mg/kg) * volume administered (mL)] / concentration of 0.007 (mL/kg).
[4] AE-Rel= Treatment-related AE. AE-NR = Nontreatment-related AE.
[5] Cumulative exposure is the sum of all doses administered.

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Programming note: if Site = "Other", concatenate specifics, "Other Injection Site"
Programming note: If entire dose not administered, concatenate specifics "Please explain why entire dose was not administered." If the dose was missed and other was selected as the reason, concatenate specifics. Reason Dose Missed is from the SAD raw dataset.

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Listing 16.2.6.1

Overall Disease Response

Dose Group	Patient Number	Best Overall Response	Date of First Occurrence of Best Overall Response/ Rel Day [1]	Best IgM Response	Type of Best IgM Response	Date of Disease Progression/ Rel Day	Date of Last Disease Assessment/ Rel Day
		CR		CR	Monoclonal		
		VGPR		VGPR	Total		
		PR		PR			
		MR		MR			
		SD		SD			
		PD		PD			
		NE		NE			

Note: Disease Response assessed by the Investigator based on the VIth International Workshop on Waldenström's Macroglobulinemia (Owen et al, 2012). CR = Complete response. VGPR = Very good partial response. PR = Partial response. MR = Minor response. SD = Stable disease. PD = Progressive disease. NE = Not evaluable.
[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.6.2

Disease Response by Visit

Dose Group	Patient Number	Visit	Date of Assessment	Rel Day [1]	Parameter	Clinical Response [2]	Overall Response [3]	Comments
					Serum Monoclonal IgM	CR	CR	
					Bone Marrow	VGPR	VGPR	
					Histology	PR	PR	
					Adenopathy	MR	MR	
					Organomegaly	SD	SD	
					Cytopenias	PD	PD	
					Symptoms	NE	NE	
					Total IgM Response	Delayed Response NA		

Note: Disease response assessed by the Investigator based on the VIth International Workshop on Waldenström's Macroglobulinemia (Owen et al, 2012).
[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] CR = Complete response. VGPR = Very good partial response. PR = Partial response. MR = Minor response. SD = Stable disease. PD = Progressive disease. NE = Not evaluable. NA = Not applicable. * Indicates best IgM response
[3] * Indicates best overall response

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Programming note: Flag the first occurrence of the best overall response. There should be one overall response per visit, and it should only print once for that visit.

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Listing 16.2.6.3A

Disease Assessment – Part 1: Lymphadenopathy and Hepatomegaly

					Physical assessment of lymphadenopathy				Physical assessment of hepatomegaly		
Dose Group	Patient Number	Visit	Date of Assessment	Rel Day [1]	Results	Region	Size (cm)	Tenderness	Results	Abnormality	Clinically Significant
					Normal			None	Normal		Yes
					Abnormal			Mild	Abnormal		No
					Not Done			Moderate	Not Done		
								Severe			

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.6.3B

Disease Assessment – Part 2: Splenomegaly

Dose Group	Patient Number	Visit	Date of Assessment	Rel Day [1]	Physical assessment of splenomegaly			
					Results	Enlarged	Palpable	Tenderness
					Normal Abnormal Not Done	Yes No	Yes No	None Mild Moderate Severe

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.6.4

Immunoglobulin (IgM) Results

					Monoclonal IgM				Total IgM			
Dose Group	Patient Number	Visit	Date of Collection	Rel Day [1]	Result (g/dL) [2]	Change from Baseline	Percent Change from Baseline	mIgM Disease Response [3]	Result (mg/dL) [2]	Change from Baseline	Percent Change from Baseline	IgM Disease Response [3]
								CR				
								VGPR				
								PR				
								MR				
								SD				
								PD				

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] * indicates Baseline value. Baseline = The most recent assessment before the first dose of study medication.
[3] CR = Complete Response. VGPR = Very Good Partial Response. PR = Partial Response. MR = Minor Response. SD = Stable Disease. PD = Progressive Disease. # indicates best IgM response.

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Programming note: IgM response taken from the database for the corresponding visit.

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Listing 16.2.6.5A

Central Tumor Laboratory Assessments – Part 1: Electrophoresis and Protein Densitometry

Dose Group: [Describe]

				By Electrophoresis						
Patient Number	Visit	Date/Time of Collection	Rel Day [1]	Albumin (unit)	Alpha-1 globulins (unit)	Alpha-2 globulins (unit)	Beta globulins (unit)	Gamma globulins (unit)	M-spike (Monoclonal IgM) (unit)	Total protein by densitometry (unit)

Note: L = Low, below normal range. H = High, above normal range.

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Programming Note: Include normal range under the lab parameter and update units. Use tumor assessments category in ADLB.

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Listing 16.2.6.5B

Central Tumor Laboratory Assessments – Part 2: Serum and Urine Assessments

Dose Group: [Describe]

				Serum							Urine		
Patient Number	Visit	Date/Time of Collection	Rel Day [1]	Protein Immuno-fixation (unit)	Serum Viscosity (unit)	Lambda FLC (unit)	Kappa FLC (unit)	FLC Ratio	Beta 2-micro-globulin (unit)	Total IgM (Immuno-globulin) (unit)	Lambda FLC (unit)	Kappa FLC (unit)	FLC Ratio

Note: FLC = Free Light Chain. L = Low, below normal range. H = High, above normal range.
[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Programming Note: Include normal range under the lab parameter and update units. Use tumor assessments, serum free light chain, and urine free light chain categories in ADLB.

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Listing 16.2.6.6

Local Tumor Laboratory Assessments

Dose Group: [Describe]

Patient Number	Visit	Date/Time of Collection	Rel Day [1]	M-spike (Monoclonal IgM) (unit)	Total IgM (Immunoglobulin) (unit)

Note: L = Low, below normal range. H = High, above normal range. * indicates result is clinically significant.
[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming Note: Use the out of range indicator from the local lab dataset (TLAL).

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Listing 16.2.6.7

Central Efficacy Laboratory Assessments: Hemoglobin and Platelets

Dose Group	Patient Number	Visit	Date of Collection	Rel Day [1]	Hemoglobin (unit)	Platelets (unit)	Patient Has Been Transfused During the Study
							Yes
							No

Note: L = Low, below normal range. H = High, above normal range.
[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Programming Note: Include normal range under the lab parameter, using central lab ranges. Use the normal range indicator in the local lab dataset for the local values. See SAP for identification of transufion status.

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Listing 16.2.6.8

Central Efficacy Laboratory Assessments: Serum NF-κB

Dose Group	Patient Number	Visit	Date of Collection	Rel Day [1]	Time Point	CD3+CD8+	CD3-CD19+	CD3-CD19+CD20+	CD3-CD19+CD23-CD10-	Comments
					Pre Dose					
					4 Hour Post Dose					

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Programming Note: Include normal range under the lab parameter if available. These data will be included in an external Excel spreadsheet.

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Listing 16.2.6.9

Immunogenicity Results: Anti-IMO-8400 Antibodies

Dose Group	Patient Number	Visit	Collection Date	Rel Day [1]	Screening Result	% Inhibition	Confirmatory Result	Titer	Comments

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Programming Note: These data will be included in an external Excel spreadsheet.

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Listing 16.2.6.10A

Serum Cytokines Test – Part 1

Dose Group	Patient Number	Date of Collection	Rel Day [1]	FGF-Basic (pg/mL)	IL-1beta (pg/mL)	G-CSF (pg/mL)	IL-10 (pg/mL)	IL-13 (pg/mL)	IL-6 (pg/mL)	IL-12 (pg/mL)	RANTES (pg/mL)	Eotaxin (pg/mL)

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Programming note: These data will be included in an external Excel spreadsheet. Include all cytokines. Create Parts 2 and 3, etc. as needed. Include normal range under the parameter if available.

Repeat for:
- Listing 16.2.6.10B Serum Cytokines Test – Part 2
- Listing 16.2.6.10C Serum Cytokines Test – Part 3
- Listing 16.2.6.10D Serum Cytokines Test – Part 4

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Listing 16.2.6.11

Bone Marrow Biopsy Results

Dose Group	Patient Number	Type of Lab	Visit	Date Sample Collected	Rel Day [1]	% Lympho-plasmacytic Lymphoma Cell Involvement	Change from Baseline	Biopsy Pathology Report	Aspirate Flow Cytometry Report	Biopsy Comment
		Central								
		Local								

Note: Baseline = The most recent assessment before the first dose of study medication.
[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.7.1

Adverse Events by Patient and MedDRA System Organ Class / Preferred Term

Dose Group:

			Onset		End									
Patient Number	SOC [1]	Preferred Term	Date/ Time	Rel Day [2]	Date/ Time	Rel Day [2]	Severity [3]	SAE	TEAE	DLT	Relationship [4]	Action Taken with IMO-8400	Action Taken for AE	Sequelae at Resolution
								Yes	Yes	Yes				Yes
								No	No	No				No

Note: SOC = System Organ Class. SAE = Serious adverse event. TEAE = Treatment-emergent adverse event. DLT = Dose limiting toxicity. CM = Concomitant medication. Adverse events coded per MedDRA version 16.1.
[1] Refer to listing 16.0.1 for the full SOC name associated with the corresponding abbreviation.
[2] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[3] 1 = Grade 1: Mild. 2 = Grade 2: Moderate. 3 = Grade 3: Marked. 4 = Grade 4: Extreme. 5 = Grade 5: Death.
[4] Relationship to Study Drug: Prob Rel = Probably Related, Poss Rel = Possibly Related, Unlike Rel = Unlikely Related, Not Rel = Not related.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If sequelae at resolution, concatenate specifics (Yes: Specify sequelae).

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Listing 16.2.7.2

Adverse Events by MedDRA System Organ Class and Preferred Term

System Organ Class:

			Onset		End									
Preferred Term	Dose Group	Patient Number	Date/ Time	Rel Day [1]	Date/ Time	Rel Day [1]	Severity [2]	SAE	TEAE	DLT	Relationship [3]	Action Taken with IMO-8400	Action Taken for AE	Sequelae at Resolution
								Yes No	Yes No	Yes No				Yes No

Note: SAE = Serious adverse event. TEAE = Treatment-emergent adverse event. DLT = Dose limiting toxicity. CM = Concomitant medication. Adverse events coded per MedDRA version 16.1.
[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] 1 = Grade 1: Mild. 2 = Grade 2: Moderate. 3 = Grade 3: Marked. 4 = Grade 4: Extreme. 5 = Grade 5: Death.
[3] Relationship to Study Drug: Prob Rel = Probably Related, Poss Rel = Possibly Related, Unlike Rel = Unlikely Related, Not Rel = Not related.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If sequelae at resolution, concatenate specifics (Yes: Specify sequelae).

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Listing 16.2.7.3

Glossary of Adverse Event Verbatim Terms by MedDRA System Organ Class, Preferred Term, and Patient

MedDRA				
SOC [1]	Preferred Term	Dose Group	Patient Number	Investigator Reported Term

Note: SOC = System Organ Class. Adverse events coded per MedDRA version 16.1.
[1] Refer to listing 16.0.1 for the full SOC name associated with the corresponding abbreviation.

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Programming Note: Sort the listing by SOC, PT, Verbatim, Dose Group, and Patient Number.

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Listing 16.2.7.4

Injection Site Reaction Assessments

Dose Group	Patient Number	Visit of Assessment	Date of Assessment	Rel Day [1]	Time of Assessment	Visit of Injection	Site of Injection	Any ISR Reported	Previous ISR for Same Site
								Yes	Yes
								No	No

Note: ISR = injection site reaction. If there was no injection site reaction noted, then further data was not recorded.
[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.7.5

Patient Reported Injection Site Reactions

Dose Group	Patient Number	Date of Assessment/ Rel Day [1]	Trait	Date of Onset/ Rel Day [1]	Date of Resolution/ Rel Day [1]	Severity	Reaction ongoing at time of assessment	Sequelae	ISR Treated
							Yes		
							No		

Note: ISR = injection site reaction.
[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Programming note: If ISR treated, concatenate specifics for con med or other treatment.

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Listing 16.2.7.6

Investigator Observed Injection Site Reactions

Dose Group	Patient Number	Date of Assessment	Rel Day [1]	Date of Injection	Visit of Injection	Trait	Status	Severity	Size (cm)	ISR Treated
						Erythema	Present	Grade 1		
						Induration	Absent	Grade 2		
						Tenderness		Grade 3		
						Pain		Grade 4		
						Pruritus		Grade 5		
						Blister		NA		
						Ulceration				
						Necrosis				

Note: NA = Not applicable. ISR = Injection site reaction.
[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Programming note: If ISR treated, concatenate specifics for con med or other treatment.

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Listing 16.2.8.1A

Central Laboratory Results: Hematology – Part 1

Dose Group: [Description]

Patient Number	Visit	Date/Time of Collection	Rel Day [1]	WBC Count (unit)	RBC Count (unit)	Hemo-globin (unit)	Hemato-crit (unit)	Platelet Count (unit)	MCH (unit)	MCHC (unit)	MCV (unit)

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
Note: RBCs = Red Blood Cells, MCH = Mean Corpuscular Hemoglobin, MCHC = Mean Corpuscular Hemoglobin Concentration,
MCV = Mean Corpuscular Volume, WBC = White Blood Cells.
L = Low, below normal range. H = High, above normal range.

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Programming Note: In all tables include normal range under the lab parameter.

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Listing 16.2.8.1B

Central Laboratory Results: Hematology – Part 2

Dose Group: [Description]

Patient Number	Visit	Date/Time of Collection	Rel Day [1]	Neutro-phils (unit)	Eosino-phils (unit)	Baso-phils (unit)	Lympho-cytes (unit)	Mono-cytes (unit)	RDW (unit)	Mean Platelet Volume (unit)	Platelet Estimate

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
Note: L = Low, below normal range. H = High, above normal range. RDW = Red Cell Distribution Width.

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Programming Note:
- Present in multiple listings as needed to present all parameters. In all central listings include normal range under the lab parameter. In local listings, there will not be a range, but use the range indicator from EDC for H or L flags. Include clinical significance if available. May need to present unit in the column (vs header), unless all observations are in the same unit for a parameter.
- For serum complement, do not include Albumin: Globulin Ratio, but add in additional parameters (C3, CH50).
- For urinalyais, add additional central urinalysis parameters to Part 5. Include RBC and WBC in Part 1. Local will have less parameters.

Repeat Listing 16.2.8.1B for:
- Listing 16.2.8.1C Local Laboratory Results: Hematology – Part 1
- Listing 16.2.8.1D Local Laboratory Results: Hematology – Part 2
- Listing 16.2.8.2A Central Laboratory Results: Chemistry – Part 1
- Listing 16.2.8.2B Central Laboratory Results: Chemistry – Part 2
- Listing 16.2.8.2C Central Laboratory Results: Chemistry – Part 3
- Listing 16.2.8.2D Local Laboratory Results: Chemistry – Part 1
- Listing 16.2.8.2E Local Laboratory Results: Chemistry – Part 2
- Listing 16.2.8.2F Local Laboratory Results: Chemistry – Part 3
- Listing 16.2.8.3A Central Laboratory Results: Urinalysis – Part 1
- Listing 16.2.8.3B Central Laboratory Results: Urinalysis – Part 2
- Listing 16.2.8.3C Central Laboratory Results: Urinalysis – Part 3
- Listing 16.2.8.3D Central Laboratory Results: Urinalysis – Part 4
- Listing 16.2.8.3E Central Laboratory Results: Urinalysis – Part 5
- Listing 16.2.8.3F Local Laboratory Results: Urinalysis – Part 1
- Listing 16.2.8.3G Local Laboratory Results: Urinalysis – Part 2
- Listing 16.2.8.3H Local Laboratory Results: Urinalysis – Part 3
- Listing 16.2.8.4A Central Laboratory Results: Coagulation
- Listing 16.2.8.4B Local Laboratory Results: Coagulation
- Listing 16.2.8.5A Central Laboratory Results: Serum Complement
- Listing 16.2.8.5B Local Laboratory Results: Serum Complement
- Listing 16.2.8.6 Local Laboratory Results: Cryoglobulins
- Listing 16.2.8.7 Local Laboratory Results: Cold Agglutinins

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Listing 16.2.8.8

Laboratory Results: Serology

Dose Group	Patient Number	Visit	Date/Time of Collection	Rel Day [1]	Lab Type	HBsAg	HIV	HCV
					Local			
					Central			

Note: HBsAg = Hepatitis B surface antigen, HIV = Human immuno deficiency virus, HCV = Hepatitis C virus.
[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Programming note: if there are local and central results, include the lab type column.

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Listing 16.2.8.9

Pregnancy Test Results

Dose Group	Patient Number	Age	Visit	Date/Time Sample Collected	Rel Day [1]	Lab Type	Test Type	Result of Pregnancy Test
						Local	Urine	
						Central		

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.9.1

Vital Signs

Dose Group	Patient Number	Date of Assessment	Rel Day [1]	Time Point	Height (cm)	Weight (kg)	SBP (mmHg)	DBP (mmHg)	Heart Rate (beats/min)	Respiratory Rate (beats/min)	Temperature (°C)	Any Abnormal, CS Results

Note: SBP = Systolic Blood Pressure. DBP = Diastolic Blood Pressure. CS = Clinically Significant.
[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.9.2

Physical Examination Findings

Dose Group	Patient Number	Date of Assessment	Rel Day [1]	Time Point	Body System	Findings

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.

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Listing 16.2.9.3

Eastern Cooperative Oncology Group (ECOG) Performance Status

Dose Group	Patient Number	Visit	Date of Assessment	Rel Day [1]	ECOG Score [2]

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] 0 = Fully active, able to carry on all pre-disease performance without restriction. 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature. 2 = Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours. 3 = Capable of only limited self-care; confined to bed or chair more than 50% of waking hours. 4 = Completely disabled. 5 = Dead.

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Listing 16.2.9.4

12-Lead Electrocardiogram Interval and Overall Assessment

Dose Group	Patient Number	Date/Time of Assessment	Rel Day [1]	Time Point	Vent-ricular Rate (bpm)	Intervals (msec) RR	PR	QRS	QT	QTc	Method	QTcF [2]	ECG Result [3]	Comment
											QTcB		Normal	
											QTcF		Ab-NCS	
													Ab-CS	

[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] If QT interval available, then QTc-Fridericia calculated. If not, then QTc Interval and Method taken from ECG Strip. QTcF is calculated using the formula QT/(RR^(1/3))
[3] ECG Result: Ab-NCS = Abnormal, Not Clinically Significant; Ab-CS = Abnormal, Clinically Significant.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

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Listing 16.2.9.5

Concomitant Medications

Dose Group	Patient Number	Medication	ATC Class / Preferred Name	Start Date/ Rel Day [1]	End Date/ Rel Day [1]	Dose	Unit	Route	Frequency [2]	Used to treat an AE	AE #

Note: ATC = Anatomic Therapeutic Classification from WHO Drug Dictionary Q12013. AE = Adverse Event.
[1] Rel Day = Calendar Days from the first dose of IMO-8400, designated day 1.
[2] BID = Twice a day, TID = Three times a day, QID = Four times a day, QD = Once a day, QOD = Every other day, QWK = Every week, Q2WK = Once every 2 weeks, Q3WK = Once every 3 weeks, QH = Every hour, Q4H = Every 4 hours, Q6H = Every 6 hours, OTO = One time only, PRN = As needed.

PROGRAM NAME: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX DATE: DDMMMYYYY HH:MM

Programming note: If medication is ongoing, enter ONGOING in end date column. If other is selected for unit, route, or frequency, concatenate specifics (Other: Specify). Update drug dictionary version if applicable.

9. REVISION HISTORY

9.1. Statistical Analysis Plan Version 2.0: 21 April 2017

Rationale of Revisions

Changes were made to the SAP to correspond with Protocol Version 7.0 dated 14 March 2016, including updates in study procedures and additional dose escalation cohorts. Changes throughout the document include minor editorial changes.

Description of Revisions Affecting Section 2

- Section 2.2.5 Safety, Efficacy, and Pharmacokinetic Parameters: Efficacy parameters were updated to include the parameters described in Protocol Section 12.4.1.2. Details of the PK parameters were removed, as they will be described in a separate report.

Description of Revisions Affecting Section 3

- Section 3.1 Population Definitions: Additional detail was added to the EE Population definition. The Safety/ITT Population was renamed to the Safety Population. The PK and PP Populations were removed.

Description of Revisions Affecting Section 4

- Section 4.2 General Methods: The relative day logic was updated to remove the flagging of the last day of treatment with an 'L' and post-treatment days with a 'P.' Detail was added for handling of missing data.

Description of Revisions Affecting Section 5:

- Section 5.2 Demographics and Baseline Characteristics: Disease history was updated to include detail of parameters included, and derivation details for IPSSWM.
- Section 5.3.1 Study Drug Exposure: Details were added to this section to include full calculations for deriving dose from the information collected on the eCRF.
- Section 5.3.2 Adverse Events: Details were added to clarify summaries are on TEAEs only. A summary of SAEs was added.
- Section 5.3.3 Laboratory Data: Details were added regarding local and central laboratory results. The listing of abnormal laboratory values was removed.
- Section 5.3.4 Vital Signs: The box plot presenting vital sign values over time was removed.
- Section 5.3.6 Electrocardiogram: Added additional tabulations of ECG data, including shift tables for QTcF and heart rate.
- Section 5.4 Efficacy Analysis:

  The following efficacy analyses were added:

  - Summary of monoclonal IgM
  - Summary of best observed response by CXCR4 mutation status
  - Summary of hematology and platelet count values

  The following efficacy analyses were removed:

  - Duration of objective response

  - Time to progression
  - Progression-free survival
  - Time to best observed response
  - Repeated measures mixed model for the change in quantitative serum levels of total IgM
  - ORR and time to progression exploratory analysis by mutation status
  - Figures for cytokine laboratory values

- Section 5.5 Pharmacokinetic Analysis: Details of the PK analysis were removed, as it will be described in a separate report.

10. APPENDICES

10.1. Appendix 1: Classification of Disease Response for Waldenström's Macroglobulinemia

Table 10.1 presents disease response categories used in this study, and is reproduced from the reference Owen et al 2008 and Protocol Section 16.2.

Table 10.1 Categorical Response Definitions

Response Category	**Definition**
Complete response (CR)	Absence of serum monoclonal IgM protein my immunofixation Normal serum IgM level Complete resolution of extramedullary disease, i.e., lymphadenopathy and splenomegaly if present at baseline Morphologically normal bone marrow aspirate and trephine biopsy
Very good partial response (VGPR)	Monoclonal IgM protein is detectable ≥ 90% reduction in serum IgM level from baseline* Complete resolution of extramedullary disease, i.e., lymphadenopathy/ splenomegaly if present at baseline No new signs or symptoms of active disease
Partial response (PR)	Monoclonal IgM protein is detectable ≥ 50% but < 90% reduction in serum IgM level from baseline* Reduction in extramedullary disease, i.e., lymphadenopathy/ splenomegaly if present at baseline No new signs or symptoms of active disease
Minor response (MR)	Monoclonal IgM protein is detectable ≥ 25% but < 50% reduction in serum IgM level from baseline* No new signs or symptoms of active disease
Stable disease (SD)	Monoclonal IgM protein is detectable < 25% reduction and < 25% increase in serum IgM level from baseline* No progression in extramedullary disease, i.e., lymphadenopathy/ splenomegaly No new signs or symptoms of active disease
Progressive disease (PD)	≥ 25% increase in serum IgM level* from lowest nadir (requires confirmation) and/or progression in clinical features attributable to the disease

* Sequential changes in IgM levels may be determined either by M protein quantitation by densitometry or total serum IgM quantitation by nephelometry

The Third International Workshop for WM also defined the following categories:

- *Not evaluable response*: Reserved for situations in which there is insufficient data for a determination of response to treatment.
- *Delayed response*: A delayed response is described particularly after treatment with purine analogue or monoclonal antibody. The recommendation was that patients should be followed for at least 2 weeks after treatment initiation to be considered unresponsive to therapy.

10.2. Appendix 2: IMO-8400 Subcutaneous Injection Site Grading (Local Reactions)

Finding	Mild	Moderate	Severe
Pain	Present; no limitations in ADL	Limitations in age-appropriate instrumental ADL *or* requires repeated non-narcotic pain reliever	Limitations in self-care ADL *or* interferes with sleep, *or* requires repeated narcotic pain reliever
Tenderness	Mild discomfort with pressure	Discomfort with touch	Discomfort elicited by clothing or bedsheets
Pruritus (itch)	Present, but minimally distracting	Present, distracting during routine activities	Interferes with sleep
Induration (swelling, edema)	Present; no limitations in ADL	Limitations in age-appropriate instrumental ADL *or* requires repeated treatment (excluding systemic steroids).	Limitations in self-care ADL *or* requires treatment with systemic steroids

Pain: discomfort or unpleasant feeling (e.g., headache) experienced while at rest or with activity; in addition to location, the patient's description may include intensity as well a distinctive quality (e.g., burning, stabbing).
Tenderness: discomfort elicited when the area is touched either intentionally or accidently.
Pruritus (itch): an unpleasant sensation that evokes the desire or reflex to scratch. (In contrast, pain and tenderness evoke a reflex to withdraw.)
Activities of daily living (ADL) are classified into two subsets:
– Instrumental ADL, e.g., preparing meals, shopping for groceries or clothes, using the telephone, managing money;
– Self-care ADL, e.g., bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not being bedridden.

10.3. Appendix 3: Intensity of AE of Injection Site Reaction

Finding	Mild	Moderate	Severe
Tenderness with or without associated symptoms (e.g., warmth, erythema, itching)	Pain; lipodystrophy; edema; phlebitis	Ulceration or necrosis; severe tissue damage; operative intervention indicated	Life-threatening consequences; urgent intervention indicated

Note: Table is based on NCI-CTCAE v.4.03. Definition of Injection Site Reaction: A disorder characterized by an intense adverse reaction (usually immunologic) developing at the site of an injection.

Pharmacokinetic Statistical Analysis Plan (PK SAP)

Protocol Title:	8400-401: Phase 1/2 Open-label, Multiple-dose, Dose-escalation Study to Evaluate the Safety and Tolerability of IMO-8400 in Patients with Relapsed or Refractory Waldenström's Macroglobulinemia 8400-402: Phase 1/2 Open-label, Multiple-dose, Dose-escalation Study to Evaluate the Safety and Tolerability of IMO-8400 in Patients with Relapsed or Refractory Diffuse Large B-cell Lymphoma and Presence of the MYD88 L265P Mutation
Investigational Drug:	IMO-8400
Protocol Number:	8400-401, 8400-402
IND Number:	119651
Sponsor:	Idera Pharmaceuticals, Inc. 167 Sidney Street, Cambridge, MA 02139, USA
Prepared By:	KinderPharm LLC 100 Arrandale Blvd. (Suite 101) Exton, PA 19341
Original Protocol Date:	**8400-401:** 11 Oct. 2013, **8400-402:** 7 March, 2014
Protocol Amendment Date:	**8400-401:** 18 Nov. 2013, 23 July 2014, 22 Sept. 2014, 25 Feb. 2015, 13 Aug. 2015, 14 March 2016 **8400-402:** 7 Nov. 2014, 12 Nov. 2014, 9 June 2015, 29 Jan. 2015
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SIGNATURE PAGE

AUTHOR

Rakesh Gollen

4/4/2017
Date

Rakesh Gollen, Ph.D.
Associate Director, Pharmacokinetics
KinderPharm LLC
100 Arrandale Blvd. (Suite 101)
Exton, PA 19341

Amir Youssef

4/7/2017
Date

Amir Youssef, Ph.D.
Director, Pharmacokinetics
KinderPharm LLC
100 Arrandale Blvd. (Suite 101)
Exton, PA 19341

REVIEWERS/APPROVERS

Martin Graham

4/7/2017
Date

Martin Graham, Ph.D.
President and CEO
KinderPharm LLC
100 Arrandale Blvd. (Suite 101)
Exton, PA 19341

4/10/2017
Date

Suzanne Swann, PhD.
Principal Statistician

Idera Pharmaceuticals, Inc.
167 Sydney Street,
Cambridge, MA 02139, USA

HISTORY LOG FOR REVISIONS MADE AFTER THE INITIAL APPROVAL

Revision Date**	**Author of Revision***	**Section(s) Modified**	**Description and/or Reason(s) Revision**

* Provide first initial and last name.

** Update the last revision dates on the cover page and the footer.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Definition
AE	Adverse Event
AUC_{0-t}	Area Under the Concentration-Time Curve from time 0 to the last time point with a concentration level ≥ LOQ
BLQ	Below the Lower Limit of Quantitation
CFR	Code of Federal Regulation
CI	Confidence Interval
C_{max}	Maximum Observed Concentration
CV	Coefficient of Variation
D	Dose
DLT	Dose-Limiting Toxicities
EOT	End-of-Treatment
EOS	End-of-Study
h	Hour
LLOQ	Lower Limit of Quantification
LOQ	Limit of Quantitation
Max	Maximum Value
Min	Minimum Value
MTD	Maximum Tolerated Dose
NCA	Non-Compartmental Analysis
PK	Pharmacokinetic(s)
PKS	Pharsight Knowledgebase Server
SAP	Statistical Analysis Plan
SD	Standard Deviation
TLFs	Tables, Listings and Figures
T_{max}	Time to reach Maximum Concentration
ULOQ	Upper Limit of Quantification

1 INTRODUCTION

1.1 Objective of the PK Statistical Analysis Plan

This statistical analysis plan (SAP) describes the planned analysis of the pharmacokinetic (PK) data from two Phase 1/2 studies (8400-401 and 8400-402). A detailed description of the tables, listings and figures (TLFs) to be presented in the stand-alone PK report for each study is provided in the accompanying TLFs shell document.

The intent of this document is to provide guidance for the analysis of the pharmacokinetic data collected as part of protocols 8400-401 and 8400-402. In general, the analyses come directly from the protocols, unless they have been modified by agreement by Idera Pharmaceuticals, Inc. A limited amount of information concerning these two studies (e.g. objectives, study design) are summarized to help the reader interpret the accompanying TLFs shell. This information is not a synopsis of the study; it is simply extracted from the protocol to guide the statistical analysis of the PK data. Attached signatures indicate approval of the PK SAP, as well as the accompanying TLFs shell. This PK SAP must be approved prior to database lock. When the PK SAP and TLFs shell are agreed upon and finalized, they will serve as the template for PK portion of the clinical study reports (CSR).

This SAP supersedes the statistical considerations identified in the protocol; where considerations are substantially different, they will be identified. If additional analyses are required to supplement the planned analyses described in this SAP they may be performed and will be identified in the appropriate section of the PK report. Any substantial deviations from this SAP will be approved by Idera Pharmaceuticals, Inc. Deviations from this SAP will be documented in the PK report.

2 STUDY OBJECTIVES

2.1 Study 8400-401

2.1.1 Primary Objective

To evaluate the safety and tolerability of escalating dose levels of IMO-8400 administered by subcutaneous (SC) injection in patients with relapsed or refractory Waldenström's Macroglobulinemia (WM).

2.1.2 Secondary Objective

• To assess the treatment effect (clinical activity) of escalating dose levels of IMO-8400 using disease-specific international guidelines for classifying clinical response.
• To identify an optimal dose of IMO-8400 for further clinical evaluation.
• To characterize the pharmacokinetics (PK) of escalating dose levels of IMO-8400

administered by SC injection.

2.1.3 Exploratory Objectives

• To investigate associations between the treatment effect of IMO-8400 and selected biomarkers (e.g., serum cytokines).
• To correlate the presence of myeloid differentiation primary response gene 88 (MYD88) L265P mutation with clinical outcome.
• To assess the potential immunogenicity of IMO-8400 administered by SC injection.

2.2 Study 8400-402

2.2.1 Primary Objective

- To evaluate the safety and tolerability of escalating dose levels of IMO-8400 administered by subcutaneous (SC) injection in patients with relapsed or refractory non-GCB subtype diffuse large B-cell lymphoma (DLBCL).

2.2.2 Secondary Objectives

- To assess the treatment effect (clinical activity) in patients with non-GCB subtype DLBCL with MYD88 L265P mutations using disease-specific international guidelines for classifying clinical response.
- To identify an optimal dose of IMO-8400 for further clinical evaluation in B-cell malignancies.
- To characterize the pharmacokinetics of escalating dose levels of IMO-8400 administered by SC injection.

2.2.3 Exploratory Objectives

- To investigate associations between the treatment effect of IMO-8400 and selected biomarkers (e.g., serum cytokines).

To assess the potential immunogenicity of IMO-8400 administered by SC injection.

3 STUDY DESIGN

3.1 8400-401

3.1.1 Study Overview

This was an open-label, multiple-dose, dose escalation study of IMO-8400 in patients with relapsed or refractory WM. The dose-escalation cohorts (3 to 6 patients each) were systematically evaluate the safety and tolerability of IMO-8400 at increasing dose levels in order to identify the maximum tolerated dose (MTD)/recommended Phase 2 dose (RP2D). The planned dose escalation

cohort levels for IMO-8400 were 0.6, 1.2, 2.4, and 3.6 mg/kg administered once weekly and 1.2 mg/kg administered twice weekly (Table 1). All dose levels (0.6 to 3.6 mg/kg/week) as SC injections were normalized by body weight at screening and advised to be recalculated if change in body weight from screening exceeds 10% (±).

Each dose-escalation cohort is expected to enroll at least 3 patients, with a maximum of 6. The criteria include: If all of the initial 3 patients complete 4 weeks of treatment without a DLT event, the DRC will conduct a dose-escalation review. If 1 of the initial 3 patients at any of these dose levels experience a DLT event prior to completing 4 weeks of treatment, then enrollment at that dose level will continue to a total of 6 patients and the dose-escalation review will be done when all 6 patients have completed 4 weeks of treatment. If 2 patients at any of these dose levels experience DLT events during the first 4 weeks of treatment, then no further patients will be enrolled until the DRC completes a review, which should be done as soon as feasible. All doses were administered by SC injection. For Dose Level 3 (refer to Table 1), the total dose was divided into 2 equal portions (1.2 mg/kg twice weekly), administered as separate SC injections over the course of the week, approximately 72 to 96 hours apart (minimum 48 hours). After establishing the safety for the 2.4 mg/kg/week as a divided weekly dose (1.2 mg/kg twice weekly), the same dose level of 2.4 mg/kg/week and subsequent dose levels were given as a once weekly administration.

The expansion cohorts provide for additional enrollment at agreed upon dose levels to assess the dose dependence of clinical response. Once the MTD or a potential RP2D and/or schedule have been established during dose escalation, up to 22 patients will be treated at the RP2D level according to this schedule. The Sponsor may decide at any point during the expansion phase to modify the RP2D based on emerging data including, but not limited to, safety, DLTs, PK, and clinical activity. If such a change is made, enrollment may continue at the selected dose level in up to 22 patients. Also, patients being treated with lower dose levels may have their doses escalated to the RP2D/MTD, after discussion and agreement between the Sponsor and the Investigator.

Screening will be done within 21 days prior to Day 1 (the first injection of study drug). Treatment is scheduled to be administered in 8-week cycles until progressive disease, unacceptable toxicity, withdrawal of consent, or end of study. Assessments for treatment response (or disease progression) are scheduled every 8 weeks ± 1 week (at the start of a new cycle) for clinical assessments, and every 4 weeks ± 1 week for laboratory assessments. End-of-Treatment (EOT) visit will be performed within 5 days of the decision to terminate treatment. End-of-Study (EOS) visit will be performed 30 to 35 days after the last dose of study drug.

Table 1: Study Design for 8400-401

Dose Level	IMO-8400 Dose (mg/kg)	Frequency	Initial Cohort Size
1 (starting dose)	0.6	Once Weekly	3 to 6
2	1.2	Once Weekly	3 to 6
3	1.2	Twice Weekly	3 to 6
4	2.4	Once Weekly	3 to 6
5	3.6	Once Weekly	3 to 6

3.2 8400-402

3.2.1 Study Overview

This is an open-label, multiple-dose, dose escalation study of IMO-8400 in patients with relapsed or refractory DLBCL of non-GCB subtype. The study is a Phase 1/2 study in which Phase 1 will consist of a dose escalation to determine the RP2D.

The dose escalation cohorts will permit systematic evaluation of the safety and tolerability of IMO-8400 at increasing dose levels in order to identify the MTD. The planned dose escalation cohort levels for IMO-8400 are 0.3, 0.6, and 1.2 mg/kg administered twice weekly and 2.4 and 3.6 mg/kg administered once weekly (**Table 2**). Additional dose levels, schedules, and routes of administration may be evaluated based upon the emerging data. Dosing is normalized to body weight, and all doses will be administered by SC injection. The Investigators and Sponsor will review available toxicity information (including adverse events [AEs] that are not DLTs), PK and clinical activity data to determine the MTD.

Table 2: Study Design for 8400-402

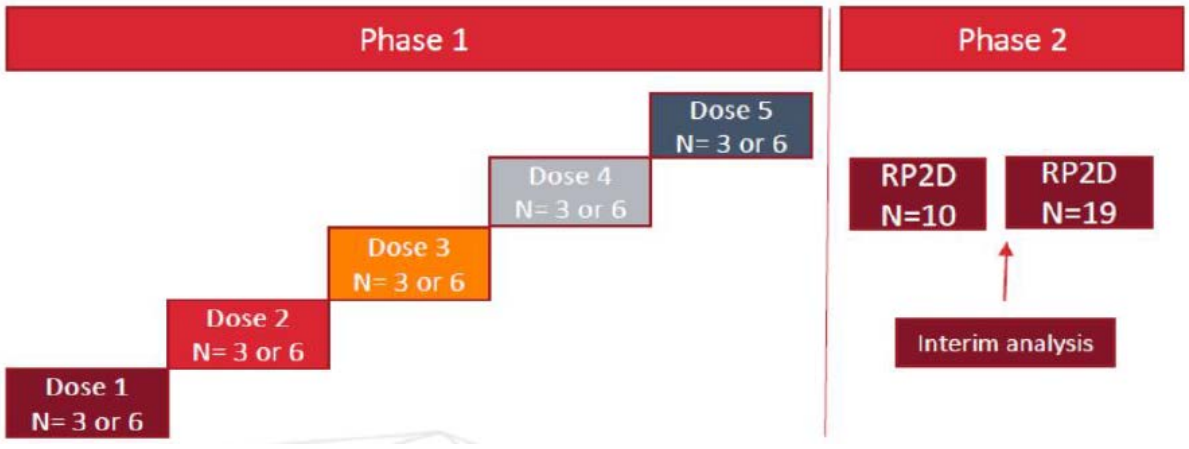
Dose Level	IMO-8400 Dose (mg/kg)	Frequency	Initial Cohort Size
1 (starting dose)	0.3	Twice Weekly	3 to 6
2	0.6	Twice Weekly	3 to 6
3	1.2	Twice Weekly	3 to 6
4	2.4	Weekly	3 to 6
5	3.6	Weekly	3 to 6

Once the RP2D has been established, additional patients will be treated in a dose expansion phase that is designed to better characterize the safety, tolerability and preliminary anti-tumor

activity of the study drug when provided at the RP2D to patients with non-GCB subtype DLBCL with MYD88 L265P mutations. Phase 2 utilizes a Simon two-stage design, consisting of an open-label treatment of patients at the RP2D. Initially 10 patients will be treated at the RP2D. If at least two of the 10 patients respond, the study will enroll 19 more patients, for a total of 29 patients in the Phase 2 portion. A schematic study design is represented in **Figure 1**.

In Phase 1, each dose escalation cohort is expected to enroll at least three patients, with a maximum of six patients. The number of patients enrolled in any of the planned dose escalation cohorts can be reduced if safety at that dose level has already been demonstrated in a related population (e.g., WM) for following reasons: 1) If the initial three patients complete all 4 weeks of treatment without a DLT event, the DRC will conduct a dose escalation review; 2) If one of the initial three patients experiences a DLT event prior to completing Cycle 1, then enrollment at that dose level will continue to a total of six patients and the dose escalation review will be done when all six patients have completed Cycle 1; and 3) If two patients at a dose-level experience DLT events during the Cycle 1, then no further patients will be enrolled until the DRC completes a review, which should be done as soon as feasible. Furthermore, cohorts may be expanded to include additional patients if such patients can be enrolled ≤7 days after the third (or sixth) patient was first dosed with IMO-8400. Screening will be done within 21 days prior to Cycle 1, Day 1 (the first treatment with study drug). The treatment is scheduled to be administered until disease progression, intolerable toxicity (despite dose modification), withdrawal of consent, start of another anti-cancer therapy, or study completion, whichever occurs first. Assessment for treatment response will continue throughout the patient's participation or until disease progression. An EOT visit will be performed within 7 days of the decision to terminate treatment. An EOS visit will be performed 30 to 35 days after the last dose of study drug.

Figure 1: Study Schematic for 8400-402



4 PHARMACOKINETIC ANALYSIS

All pharmacokinetic analyses and generation of TLFs will be performed using a validated installation of Phoenix WinNonlin® version 6.4 (Pharsight, Cary, North Carolina USA) as part of a 21 CFR Part 11 compliant database system (Pharsight Knowledgebase Server "PKS").

4.1 PK Population

The primary analysis of PK will be conducted on the Pharmacokinetic (PK) Population which includes all patients who had both a pre-dose and at least one analyzable post-dose PK sample.

4.2 Blood Sampling Schedule

4.2.1 8400-401

Pharmacokinetic samples (2 mL blood volume) will be obtained as scheduled in relation to first weekly dose administered on Day 1 of every cycle, at pre-dose and at 1 (± 5 minutes), 2 (± 10 minutes), and 4 (± 15 minutes) hours post-dose. A PK sample will also be collected at the EOT and EOS visits. Plasma samples will be analyzed for IMO-8400 concentration using a validated bioanalytical method. Pharmacokinetic analysis will be conducted on an individual basis. The actual time and date of each blood draw will also be reported.

4.2.2 8400-402

Pharmacokinetic samples (5 mL blood volume) will be obtained as scheduled in relation to the first dose administered at each of Cycles 1, 2, 4, and 6 (Day 1 of each cycle). The following PK samples will be collected: pre-dose, at 1 (±5 minutes), 2 (±10 minutes), and 4 (±15 minutes) hours post-dose. Pharmacokinetic samples will also be collected at the EOT and EOS visits. Plasma samples will be analyzed for IMO-8400 concentration using a validated bioanalytical method.

4.3 Pharmacokinetic Parameters

4.3.1 8400-401

For each cohort, the plasma IMO-8400 concentration data will be analyzed by non-compartmental PK analysis. The following parameters (Table 3) will be determined as appropriate: observed maximum plasma concentration (C_{max}), time of C_{max} (T_{max}), and AUC from 0 to last measurable plasma concentration (AUC_{0-t}). Pharmacokinetic parameters will be compared across IMO-8400 dose levels. Descriptive statistics will be provided for all PK parameter values by dose and time, as appropriate.

4.3.2 8400-402

For each cohort, the plasma IMO-8400 concentration data will be analyzed by non- compartmental PK analysis. The following parameters (Table 3) will be determined as appropriate: observed maximum plasma concentration (C_{max}), time of C_{max} (T_{max}), and area under the curve from 0 to last measurable plasma concentration (AUC_{0-t}). Pharmacokinetic parameters will be compared across IMO-8400 dose levels. Descriptive statistics will be provided for all PK parameter values by dose and time, as appropriate.

Table 3. Planned Non-Compartmental PK Parameters.

Parameter	Description of Parameter
C_{max}	Maximum observed concentration.
T_{max}	Time of the maximum observed concentration.
AUC_{0-t}	The area under the concentration time course profile from time = 0 (dosing) to the last quantifiable concentration (C_t) will be estimated using the linear trapezoidal rule follows: $$AUC_{0-t} = \sum_{i=1}^{n-1}\left[\frac{C_{i+1}+C_i}{2}(t_{i+1}-t_i)\right]$$ Where C_i is the *i*-th sample, t_i is the time of the *i*-th sample from dosing, and n is the number of available samples up to and including the final quantifiable concentration.

AUC values will be estimated using the linear trapezoidal rule. Actual sampling times relative to dosing will be used in the computation.

4.4 Handling of Missing Sampling or Concentration Data

Unless otherwise specified below, missing sampling or concentration values will not be imputed, but left missing in the calculation of derived PK parameters. Concentrations that are not reportable due to technical artifact or ambiguity (such as described in Section 4.6) will be treated as missing values. If the actual sampling time is missing, but a valid concentration value has been measured, the scheduled protocol time will be used for the calculation of derived PK parameters. A missing pre-dose value will be set to 0 for the PK calculations corresponding to an observation at dosing time (C_0).

4.5 Handling of Concentration Values below the Limit of Quantification (BLQ)

For calculation of PK parameters, concentrations that are BLQ prior to or after the T_{max} will be set to 0. For calculation of concentration summary (e.g., mean concentration), concentrations that are BLQ will be set to 0.

4.6 Handling of Outliers

On a case by case basis, it may be necessary to exclude individual bioanalytical data from the calculation of derived PK parameters because they are erroneous, abnormal or appear implausible to the pharmacokineticist in charge of the analysis. Any excluded data will be flagged in the individual data listings. The reason for exclusion will also be documented. If the exclusion has a meaningful impact on the overall interpretation of the results, then it will be discussed.

4.7 Handling of Actual vs. Planned Sampling Timepoints

Actual post-dose time will be used in calculation of PK parameters and in the generation of individual concentration-time profiles. Scheduled (nominal) sampling times will be used as a replacement for unknown or missing actual times and will be used for the pre-dose values. Nominal sampling times will also be used in the generation of summary concentration-time plots and tables

4.8 Handling of Individual Data and Summary Data Formats

The actual values as provided from the bioanalytical laboratory will be displayed as individual concentration-time listings. Study drug concentrations will be used to calculate the following parameters: C_{max}, T_{max}, and AUC_{0-t}, using non-compartmental analysis. For summary tables, the descriptive statistics will be rounded to one more digit than the individual values for the arithmetic mean, SD, median and geometric mean, and to the same number of digits for the minimum and maximum values. The T_{max} will be reported using the median and range up to 2 decimal points in listing and summary tables. The number of non-missing observations (N) will be reported as an integer number. The CV% and geometric CV% will be reported as a percentage of the integer number.

5 STATISTICAL METHODS

5.1 General Statistical Considerations

Statistical analysis will be conducted by Kinder-Pharm LLC, using Phoenix WinNonlin 6.4 or newer version (Pharsight, Cary, North Carolina USA).

5.2 Statistical Assessment

A nonlinear power model will be used to assess the dose proportionality of IMO-8400 on day 1 of cycle 1 and cycle 2. The proportional relationship between exposure (C_{max}, AUC_{0-t}) and dose will be evaluated as a power model as follows:

$$\text{Parameter} = A \cdot \text{dose}^{B}$$

where A is a constant, B is the proportionality co-efficient, and the parameter is C_{max} and AUC_{0-t}. In conducting this analysis, the power model will be converted to a linear mixed effect model using natural logarithmic transformation as follows:

$$\ln(\text{parameter}) = \ln(A) + B*\ln(\text{dose})$$

If the 90% confidence interval for the slope (B) includes 1.0, then the relationship will be considered to be dose proportional.

6 PRESENTATION OF RESULTS

6.1 Listings

Individual time course values (nominal and actual sampling timepoints) and plasma IMO-8400 concentrations will be listed for all subjects for each study separately (8400-401, and 8400-402). Individual IMO-8400 plasma PK parameter estimates from non-compartmental analysis will be listed for the PK Population. The PK parameters will include C_{max}, and T_{max}, and AUC_{0-t}.

6.2 Tables

Descriptive summary statistics (number of non-missing observations (N), arithmetic mean, standard deviation (SD), coefficient of variation (CV), median, minimum, maximum) will be reported for concentration profiles, grouped by each cohort (dose level) and each cycle (visit) and treatment for each study separately (8400-401 and 8400-402).

Descriptive summary statistics (number of non-missing observations (N), arithmetic mean, standard deviation (SD), median, minimum, maximum, range, geometric mean and geometric CV% will be reported for PK parameters (C_{max}, T_{max}, and AUC_{0-t}), grouped by cohort and each cycle (visit) for each study separately (8400-401, and 8400-402). All descriptive statistics will be reported for untransformed PK parameters.

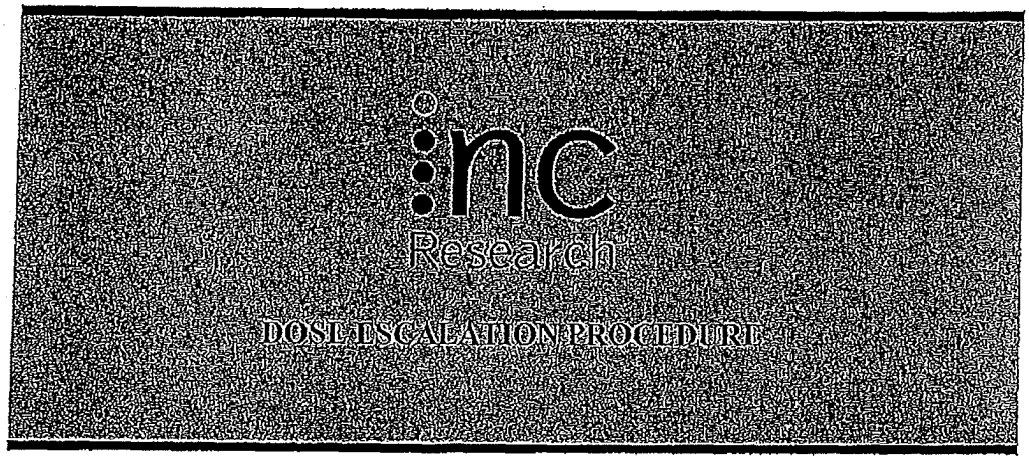
Geometric mean of C_{max} and AUC_{0-t} of cycle 1 day 1, and cycle 2 day 1 will be tabulated by dose to facilitate dose proportionality assessments. Dose-proportional power model analysis tables for C_{max} and AUC_{0-t} will be presented as the parameters Ln (A) and B, along with the respective 90% CIs.

6.3 Figures

Individual plots: The time course of IMO-8400 plasma concentration profile will be presented as one plot per graph and as composite plots for all subjects for each dose separately for each study separately (8400-401, and 8400-402). The graphical output will be presented in both linear and semi-log scales. Actual sampling times will be used for individual plots.

Mean plots: For each study separately (8400-401, and 8400-402), the arithmetic mean of IMO-8400 plasma concentration time profiles sorted by cohort and cycle will be presented in linear and semi-log graphs for each dose group. Linear mean plots will be presented with their upper SD bars. Scheduled (nominal) sampling times will be used for mean plots.

Linear regression plot: Evaluable IMO-8400 C_{max} and AUC_{0-t} of cycle 1 and cycle 2 versus dose will be presented for each study separately (8400-401, and 8400-402). Linear regression line, R-squared (Rsq), intercept, and slope will also be reported.



Sponsor	Idera Pharmaceuticals, Inc.
Protocol Number	8400-401
Protocol Title	Phase 1/2 Open-label, Multiple-dose, Dose-escalation Study to Evaluate the Safety and Tolerability of IMO-8400 in Patients with Relapsed or Refractory Waldenström's Macroglobulinemia
INC Research Project Code	1004040
Version	3.0
Date:	23-Jun-2016

APPROVALS INC Research©	
Nicole Pusey, Project Lead	28 Jun 2016 Date
Jane Bullock, Clinical Team Lead	29 Jun 2016 Date
Robert Gazak, Project Director	29 Jun, 2016 Date
Idera Pharmaceuticals	
Lindsey Simov, Sr. Clinical Trial Manager	30 Jun 2016 Date
Mark Cornfeld, M.D., VP & Medical Lead, Oncology	30 Jun 2016 Date

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1. REVISION HISTORY

Version*	Date	Document Owner	Revision Summary
1.0	07-Jul-2014	Project Lead	Initial Dose Escalation Procedure Plan
2.0	15-Sep-2014	Project Lead	Updated Data Review Committee Members Chart
3.0	23-Jun-2016	Project Lead	Added Revision History Table Updated signatories Addition of Veristat's responsibilities Included anticipated outcomes from protocol Added appendix to list participating investigators

* Note: Updates to appendices will be handled and filed independently and do not require an update and re-signing of the Dose Escalation Procedure Plan in its entirety.

2. DATA REVIEW COMMITTEE (DRC) MEMBERS

Affiliation	Name / Position	Contact Information
Participating Investigators	Please see Appendix 1	Please see Appendix 1
Medical Monitor	Mark Cornfeld, MD VP & Medical Lead, Oncology Idera Pharmaceuticals, Inc.	T: 484-348-1629 M: 609-240-7312 E: mcornfeld@iderapharma.com

3. OBJECTIVE

The objective of this document is to establish the responsibilities and the procedure for handling of the patient safety data and the organization of the Data Review Committee (DRC) - to allow the Sponsor and participating investigators to evaluate preliminary safety data make a recommendation for the dose level to be used in the next cohort of patients, maximum tolerated dose (MTD) or other appropriate action.

4. PROTOCOL

Protocol Number: 8400-401

Protocol Title: "A Phase 1/2 Open-label, Multiple-dose, Dose-escalation Study to Evaluate the Safety and Tolerability of IMO-8400 in Patients with Relapsed or Refractory Waldenström's Macroglobulinemia"

5. RESPONSIBILITIES

5.1 Investigator

The primary responsibility of the Investigator at all times is the safety of the individual patient. Per protocol, the investigators responsibilities include the following:

- Monitor patients for adverse events, including laboratory abnormalities, with particular attention to those meeting the criteria for a serious adverse event and dose-limiting toxicity (DLT) as defined in the protocol.
- Document and enter study procedure and safety data in the Electronic Case Report Form (eCRF) in a timely manner, typically within 48 hours. All relevant eCRF pages (including safety pages) - for the patients that will be discussed during the upcoming dose escalation teleconference must completed within 48 hours after the last patient of the cohort has completed the DLT period. (i.e., received four weeks of treatment and completed the Week 5 visit procedures).
- If requested, participate in the dose escalation teleconferences and provide patient updates.

5.2 INC Research

- Monitor the sites at regular intervals and check the patient files with particular attention to safety data (CRA). Whenever possible, monitoring visits will be scheduled close to the upcoming DRC meeting so that as much of the data as possible has been monitored.
- Organize the DRC meeting as close as possible to completion of DLT period of last patient in the cohort and provide the following support: schedule meeting date and time, prepare agenda, prepare meeting minutes, and file any related documents in the Electronic Trial Master File (eTMF).
- The following INC Research project team members will participate in the DRC meeting: Project Manager, Lead CRA, Project Specialist.

5.3 Data Management (Axiom)

- Distribute patient safety data listings to committee members.

5.4 Veristat

- If necessary, provide patient safety data listings based on information available in the trial database in an agreed upon format at least 2 days prior to the scheduled DRC meeting. These listings may include data that has not yet been monitored.

5.5 Sponsor

- Monitor subject eligibility by reviewing all screening data to confirm enrollment parameters are met.
- Review of available patient safety data listings provided prior to each DRC meeting.

- Review/approval of the DRC meeting minutes before distribution to all participants.
- The following Sponsor representatives who will participate in the DRC meeting include, but are not limited to:
  Idera Medical Monitor and Clinical Trial Manager
- ***While the DRC will review data and make specific recommendations as detailed below, the final decision (e.g., dose escalate to the next higher dose level, de-escalate to a contingency dose level, or establish the MTD) will be made by Idera Pharmaceuticals, Inc and communicated by their representative.***

6. PREPARATION FOR DOSE ESCALATION MEETINGS

The information needed for the DRC review includes the following elements:

- Demographics
- Inclusion Criteria
- Exclusion Criteria
- Dose Level Assignment
- Dosing
- Adverse Events
- Injection Site Assessments
- Concomitant Medications
- Laboratory Assessments

The INC PM or designee will perform the following:

- Set a meeting date and time at least three weeks in advance
- Prepare a meeting agenda, including the appropriate dial-in numbers and teleconference code.
- Distribute the meeting agenda to all DRC attendees at least one week in advance.

Axiom and/or Veristat will perform the following:

- Prepare the data safety listings for distribution to all DRC members at least 48 hr prior to the meeting.

7. CONDUCT OF DOSE ESCALATION MEETINGS

DRC meetings will be scheduled per the dose escalation enrollment and review guidelines outlined in the protocol. The INC Project Manager (PM) will co-ordinate the DRC meetings. Each DRC member will have the opportunity to comment on the data presented, request additional data (if available), and offer their medical judgment regarding implications for the safety of patients enrolled in this study. As noted in the protocol, decisions regarding dose escalation will primarily be based on toxicities seen during the first four weeks of treatment to facilitate consistency across cohort, adverse events occurring beyond that period may be discussed and considered.

The goal of the discussion is to reach a consensus recommendation regarding:

- Review and provide definitive adjudication on individual DLTs, if needed
- Perform dose-escalation review and make specific recommendations for the progress of the study
- Determine the MTD / RP2D, or another dose for further exploration

However, if consensus is not possible, then individual members may offer specific alternative recommendation(s) that are consistent with the protocol.

The following represent anticipated outcomes for the review process:

- Dose escalation – progression to the next planned dose level.
- Continue cohort enrollment (applicable only to review after 3 patients) – enroll up to 6 patients at the current dose level to obtain additional safety data for subsequent review.
- Dose de-escalation – enrollment of intermediate dose levels for exploration of other schedules of administration.
- Approve enrollment in an expansion cohort at a selected dose level, if applicable (see Section 6.4).
- No further dose escalation enrollment – at this time the DRC will indicate the dose level that they consider represents the MTD.

In the event that a principal investigator is not able to attend the DRC meeting, then that principal investigator may indicate agreement with the DRC outcome / decisions via email. Any agreements via email will be documented and filed with the DRC minutes.

As noted above, the final decision remains the responsibility of Idera.

8. OUTCOME OF DOSE ESCALATION MEETINGS

Minutes will be prepared by INC Research PM/PC and shall include:

- DLT events identified and confirmed by the DRC
- Other treatment-related adverse events discussed by the DRC
- The consensus recommendation and individual alternative recommendations, if any.

The minutes will be provided to the Sponsor within 48 hours of the DRC meeting. The Sponsor will review the minutes, add their decision regarding study progression, and then distribute the minutes to all other attendees within another 48 hours. If the Sponsor's decision diverges from the DRC recommendation, a follow-up conference call may be scheduled to permit further discussion.

9. APPENDIX

The appendix can be revised without the full review and written approval of the Dose Escalation Procedure. Appendix version control is required.

9.1 Appendix 1 – Investigator Contact List

Site No	Last Name	First Name	Company	Business Address	Business Phone	Business Fax	E-mail
501	Thomas	Sheeba	MD Anderson Cancer Center	1515 Holcombe Blvd. Houston, TX 77030	713-792-2860	713-744-5656	sthomas@mdanderson.org
504	Harb	Wael	Horizon BioAdvance	1345 Unity Place Suite 365 Lafayette, IN 47905	765-446-5165	765-838-0972	wharb@horizonbioadvance.com
505	Vesole	David	Hackensack Unviersity Medical Center	92 Second Street Hackensack, NJ 07601	551-996-8704	551-996-0582	dvesole@hackensackUMC.org
506	Ansell	Stephen	Mayo Clinic	200 First Street SW Rochester, MN 55905	507-284-2511	507-284-5280	ansell.stephen@mayo.edu
509	Beck	Joseph	Highlands Oncology Group	3232 N. North Hills Blvd. Fayetteville, AR 72703	479-587-1700	479-587-1366	tbeck@hogonc.com
511	Eradat	Herbert	UCLA Medical Center	10945 Le Conte Ave., Suite 3360 Los Angeles, CA 90095	310-709-7741	N/A	heradat@mednet.ucla.edu
512	Heffner	Leonard	Emory University	1365 Clifton Rd. Bldg. C Suite 3012 Atlanta, GA 30322	404-778-1900	404-778-4389	lheffne@emory.edu
513	Libby	Edward	Fred Huchison Cancer Center	825 Eastlake Ave E. LV-200 Seattle, WA 98109	206-288-1453	206-288-6549	elibby@seattlecca.org