Integrated Analysis Plan

Clinical Trial Protocol Identification No.	MS201923-0007
Title	A Rollover Study to Provide Continued Treatment with M6620
Trial Phase	I
Investigational Medicinal Product(s)	M6620
Clinical Trial Protocol Version	08 September 2017 / Version 2.0
Integrated Analysis Plan Author	**Coordinating Author** PPD, Merck PPD **Function** / **Author(s) / Data Analyst(s)** PPD PPD
Integrated Analysis Plan Date and Version	28 January 2019 / Version 1
Integrated Analysis Plan Reviewers	**Function** / **Name** PPD PPD PPD, Merck PPD PPD, Merck PPD

Approval Page

Integrated Analysis Plan: MS201923-0007

A Rollover Study to Provide Continued Treatment with M6620

Merck responsible	Date	Signature
PPD	Via ELDORADO approval process	

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2 List of Abbreviations and Definition of Terms

AE	Adverse Event
eCRF	Electronic Case Report Form
ENR	Enrolled Analysis Set
IAP	Integrated Analysis Plan
ICH	International Conference on Harmonization
MedDRA	Medical Dictionary for Regulatory Activities
NCI-CTCAE	National Cancer Institute – Common Terminology Criteria for Adverse Events
SAE	Serious Adverse Event
SAF	Safety Analysis Set
SDTM	Study Data Tabulation Model
WHO-DD	World Health Organization-Drug Dictionary

3 Modification History

Unique Identifier for Version	Date of IAP Version	Author	Changes from the Previous Version
1.0	28Jan2019	PPD	Initial version.

4 Purpose of the Integrated Analysis Plan

The purpose of this Integrated Analysis Plan (IAP) is to document technical and detailed specifications for the presentation of data collected for protocol MS201923-0007.

The IAP is based upon Section 8 (Statistics) of the trial protocol and protocol amendments and is prepared in compliance with International Conference on Harmonization (ICH) E9.

5 Objectives and Endpoints

	Objective	Endpoint	IAP section
Primary Objective	To monitory safety of subjects that are on long-term treatment with M6620.	Occurrence adverse events (AEs) in subjects receiving M6620, graded according to National Cancer Institute Common Terminology Criteria for AEs (NCI-CTCAE) (Version 4.03), 28 days after the last administration of M6620.	15.1

6 Overview of Planned Analyses

There are no interim analyses planned for this study. All final, planned analyses identified in the Clinical Trial Protocol and in this IAP will be performed only after the last subject has completed the study with all trial data in-house, all data queries resolved, and the database locked.

A data review meeting will be held prior to database lock. In addition, no database can be locked until this IAP has been approved.

7 Changes to the Planned Analyses in the Clinical Trial Protocol

Due to the small number of subjects on the study, no statistical analysis will be conducted, and the data will be presented in listings only.

8 Protocol Deviations and Analysis Sets

The following populations are defined per protocol.

Enrolled analysis set (ENR): All subjects who sign informed consent for this study.

Safety analysis set (SAF): All subjects who receive at least 1 dose of study drug in this study. Subjects will be analyzed according to the actual treatment they receive.

9 General Specifications for Data Analyses

All data will be listed as collected, and no derived datasets will be produced. All listings will be based upon the Study Data Tabulation Model (SDTM) datasets. Subjects will be listed according to the cohort in which they were continued from the previous study.

10 Trial Subjects

10.1 Disposition of Subjects and Discontinuations

Subject disposition and treatment/trial discontinuation data will be listed as collected on the electronic case report form (eCRF).

10.2 Protocol Deviations

All important deviations from inclusion/exclusion criteria will be listed.

11 Demographics and Other Baseline Characteristics

All demographic and baseline characteristics data will be listed as collected on the eCRF.

12 Concomitant Medications/Procedures

Concomitant medications, as reported on the eCRF, will be listed according to the Anatomical Therapeutic Class (ATC) Level 2 text and preferred term as given from the current version of the World Health Organization-Drug Dictionary (WHO-DD) dictionary at time of database lock and noted as to whether they were ongoing at the time of study transition.

Concomitant procedures will be listed according to the reported name and standardized name as given from the current version of the Medical Dictionary for Regulatory Activities (MedDRA) dictionary at the time of database lock.

13 Treatment Compliance and Exposure

All exposure data will be listed, as collected on the eCRF, by the drug administered.

14 Efficacy Analyses

Not applicable.

15 Safety Analyses

All safety data will be listed as collected on the eCRF.

15.1 Adverse Events

All adverse events (AEs) will be listed according to the preferred term as given from the current version of the MedDRA dictionary at the time of database lock. All serious adverse events (SAEs) will be noted in the main AE listing, and a separate SAE listing will be produced.

15.2 Clinical Laboratory Evaluation

Clinical laboratory results will be listed with the applicable normal ranges along with flags for above/below normal range.

15.3 Vital Signs

All vitals sign results and subject weights will be listed as collected on the eCRF.

16 References

Not applicable.

17 Appendices

Not applicable.