Study information

Title	Real-World (RW) Elranatamab Administration: Step Up Dosing (SUD), Treatment Patterns, and Healthcare Resource Utilization (HCRU) in Japan MDV Data (SUMMIT)
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Active substance	L01FX32
Medicinal product	ELREXFIO™ (elranatamab)
Research question and objectives	**Research Question:** What are the characteristics of adult patients with MM who initiate elranatamab in Japan, and the SUD process, treatment patterns, HCRU, and safety associated with elranatamab administration? The following objectives will be assessed among patients with MM receiving elranatamab: **Primary objectives:** • Objective 1: To describe patients with MM initiating elranatamab, including demographics, treatment and medical history. • Objective 2: To describe and characterize elranatamab utilization, including timing, administration and dosing, during the follow-up period, including the step-up dosing (SUD) period. **Secondary objectives:** • Objective 3: To describe HCRU and costs associated with elranatamab usage during the follow-up period, including the SUD period. • Objective 4: To describe the use of other treatments for MM including supportive therapy during the follow-up period. • Objective 5: To describe incidence and prevalence of cytokine release syndrome (CRS), immune effector cell associated neurotoxicity syndrome (ICANS), and cytopenias during the SUD period.

	• *Objective 6:* To describe infection incidence and prevalence during the follow-up period. **Exploratory objectives:** • Exploratory Objective 1: To describe the use of supportive medications during the SUD period and administration of IVIG within the 30-day post-index period.
Country(ies) of study	Japan
Author	[redacted]

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2. LIST OF ABBREVIATIONS

Abbreviation	Definition
ADL	Activity of Daily Living
AE	Adverse event
anti-CD38	Anti-CD38 Monoclonal Antibodies
BCMA	B-cell Maturation Antigen
BM	Bone Marrow
CAR-T	Chimeric Antigen Receptor T-cell
CCI	Charlson Comorbidity Index
CIOMS	Council for International Organizations of Medical Sciences
CM	Centimeter
CRS	Cytokine release syndrome
DPC	Diagnosis Procedure Combination
EC	Ethics Committee
ED	Emergency Department
EU	European Union
GDPR	General Data Protection Regulation
GPP	Guidelines of Good Pharmacoepidemiology Practices
HCPCS	Healthcare Common Procedure Coding System
HCRU	Healthcare Resource Utilization
ICANS	Immune effector Cell Associated Neurotoxicity Syndrome
ICD-10	International Classification of Diseases, 10th revision
IMiD	Immunomodulatory Imide Drug
IP	Inpatient
IQR	Interquartile range
IRB	Institutional Review Board
ISPE	International Society for Pharmacoepidemiology
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
ISS	International Staging System

IVIG	Intravenous immunoglobulin
LB	Pound
MDV	Medical Data Vision
MM	Multiple Myeloma
NI	Non-Interventional
OP	Outpatient
OS	Overall Survival
PASS	Post-Authorization Safety Study
PI	Proteasome Inhibitor
PMDA	Pharmaceuticals and Medical Devices Agency
PPPD	Per Patient Per Day
PPPM	Per Patient Per Month
QW	Once weekly
Q2W	Once every two weeks
RAI	Relative Administration Intensity
RRMM	Relapsed/Refractory Multiple Myeloma
RW	Real-World
RWD	Real-World Data
SAP	Statistical Analysis Plan
SCT	Stem cell transplantation
SD	Standard Deviation
SUD	Step-Up Dosing
TCE	Triple-class exposed

3. RESPONSIBLE PARTIES

Principal Investigator(s) of the Protocol

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[redacted]	[redacted]	[redacted]	[redacted]

4. ABSTRACT

- **Title:** Real-World (RW) Elranatamab Administration: Step Up Dosing (SUD), Treatment Patterns, and Healthcare Resource Utilization (HCRU) in Japan MDV Data (SUMMIT)

  Version: 2.0

  Date: 15 September 2025

  [redacted]

- **Rationale and background:** Despite treatment advancements, many MM patients experience relapse or refractory disease (RRMM), leading to poor prognosis and limited options. Elranatamab is the first bispecific B-cell maturation antigen (BCMA)-directed monoclonal antibody to receive approval from the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) in March 2024. Elranatamab was approved for the treatment of patients with RRMM who have been exposed to at least three standard therapies including IMiD, PI, and anti-CD38, i.e. triple-class exposed (TCE). This study will leverage a Japanese hospital-based administrative health dataset to describe the RW administration of elranatamab, including patient selection, treatment patterns and healthcare utilization (HCRU) in an MM population.

- **Research question and objectives:**

  Research question: What are the characteristics of adult patients with MM who initiate elranatamab in Japan, and the SUD process, treatment patterns, HCRU, and safety associated with elranatamab administration?

  The following objectives will be assessed among patients with MM receiving elranatamab:

  Primary objectives:

  Objective 1: To describe patients with MM initiating elranatamab, including demographics, treatment and medical history.

  Objective 2: To describe and characterize elranatamab utilization, including timing, administration and dosing, during the follow-up period, including the step-up dosing (SUD) period.

  Secondary objectives:

  Objective 3: To describe HCRU and costs associated with elranatamab usage during the follow-up period, including the SUD period.

  Objective 4: To describe the use of other treatments for MM including supportive therapy during the follow-up period.

  Objective 5: To describe incidence and prevalence of cytokine release syndrome (CRS), immune effector cell associated neurotoxicity syndrome (ICANS), and cytopenias during the SUD period.

  Objective 6: To describe infection incidence and prevalence during the follow-up period.

Exploratory objectives:

Exploratory Objective 1: To describe the use of supportive medications during the SUD period and administration of IVIG within the 30-day post-index period.

- **Study design:** This is a retrospective observational study utilizing de-identified data from Japan Hospital administrative claims data (Medical Data Vision [MDV]).

- **Population:** The study population will include all adults aged 18 years or older with an MM diagnosis who initiate elranatamab on or after March 26, 2024 (PMDA Elrexfio approval date). Patients with evidence of clinical trial participation will be excluded.

- **Variables**: The following variables will be summarized and reported:

Exposure of interest:

Exposure is defined as at least one record of a hospital claim for elranatamab on or after March 26, 2024. All patients included in the study will be considered exposed. Analyses of outcomes during the SUD period will also be stratified based on types of elranatamab exposure during that time (i.e., complete and timely SUD, complete but not timely SUD, alternative SUD). Clinical data will be collected from MDV hospital data.

Study outcomes:

Study endpoints include: elranatamab timing and dosing (i.e., types of doses, time between doses, relative administration intensity), HCRU and costs (i.e., IP/OP/ED claims and associated costs, degree of nursing), other MM treatment post elranatamab administration (i.e., PIs, SCT, supportive therapy), known adverse events (i.e., CRS events occurrence, frequency and associated length of stay, time from index to CRS event), infection (i.e., infection occurrence, time from index to infection, antibiotics), and supportive medication (i.e., IVIG, acetaminophen, dexamethasone).

Covariates:

Covariates will include baseline demographics (i.e., age, sex, weight etc.), and baseline clinical characteristics (i.e., comorbidities and treatment history).

- **Data sources**: The MDV database is a comprehensive resource containing administrative data from over 540 hospitals in Japan. This dataset includes information on demographics, mortality, labs, IP, OP, ED claims, treatments, procedures and costs of approximately 50 million patients. MDV is an aggregated, de-identified dataset where no patient can be individually identified and therefore no patient consent is required.

- **Study size:** This is a retrospective descriptive study with no a priori hypotheses; therefore, sample size calculations are not applicable. As of February 2025, MDV included 128 patients that had at least one hospital claim for an elranatamab administration.

- **Data Analysis:** Descriptive statistics will be used for all objectives, and no hypothesis testing will be conducted. Incidence and prevalence calculations will be conducted.

- **Milestones:** The study will be registered in the HMA-EMA Catalogues of RWD studies on July 14, 2025, followed with data collection commencing on July 15, 2025. An interim study analysis is scheduled for release on September 30, 2025. Data collection will conclude on June 30, 2026, followed by the final study report on November 30, 2026.

5. AMENDMENTS AND UPDATES

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section(s) Changed	Summary of Amendment(s)	Reason
2.0	15 September 2025	Substantial	6. Milestones	Update milestones, interim report was removed and replaced with interim analysis	Reflective of revised project deliverables
2.0	15 September 2025	Substantial	9. Research Methods • 9.1. Study Design • 9.2. Setting • 9.3. Variables • 9.7. Data analysis	- Additional assessment periods for adverse events (Obj. 5) and supportive medication assessment (Exploratory Obj. 1) - Clarified definitions of existing variables with additional data information - Added new variables of interest for Objective 2 (i.e., addition of variables of interest at a patient and claim level), and Objective 5 (i.e., concomitant medication at the same time as the AE event).	- Enhance data granularity following clinical input. - Improvement of consistency with data - Capture additional data relevant to the study objectives
2.0	15 September 2025	Substantial	9.7.5. Subgroup analysis	A subgroup analysis was added for low weight patients receiving elranatamab.	Provide deeper insights into treatment outcomes and safety within this specific patient population,

6. MILESTONES

Milestone	Planned Date
Start of data collection	15 July 2025
End of data collection	30 June 2026
Interim analysis	30 September 2025
Registration in the HMA-EMA Catalogues of RWD studies	15 July 2025
Final study report	30 November 2026

7. RATIONALE AND BACKGROUND

Multiple myeloma (MM) is a hematologic malignancy characterized by an excess of monoclonal bone marrow (BM) plasma cells. In Japan, it is estimated that MM has an incidence rate of 5.8 cases and a death rate per capita of 3.5 per 100,000 people (1). Though its incidence has increased over recent years, the mortality rates have decreased – coinciding with the introduction of novel therapies (2).Historically, treatment options for patients with MM were limited to a combination of alkylating agents, such as melphalan, and steroids such as prednisone (3,4). However, the development of new therapies has led to profound changes in the treatment landscape and has increased overall survival (OS) in patients with MM especially with the approval of therapies designed to target specific pathogenic pathways, including the following: proteasome inhibitors (PIs) (carfilzomib, ixazomib, and bortezomib), immunomodulatory imide drugs (IMiDs) (pomalidomide, thalidomide, and lenalidomide), and anti-CD38 monoclonal antibodies (anti-CD38) (daratumumab, daratumumab and hyaluronidase-fihj, and isatuximab-ifrc) (5).

Despite treatment advancements, many MM patients experience relapse or refractory disease (RRMM), leading to poor prognosis and limited options. Elranatamab is the first bispecific B-cell maturation antigen (BCMA)-directed monoclonal antibody to receive approval from the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) in March 2024. Elranatamab was approved for the treatment of patients with RRMM who have been exposed to at least three standard therapies including IMiD, PI, and anti-CD38, i.e., triple-class exposed (TCE).

Results from MagnetisMM-2 and MagnetisMM-3 reported common adverse events (AE) to be CRS, ICANS, cytopenia, and infections (6,7).A past study sponsored by Pfizer compared Japanese patients in MagnetisMM-2 and MagnetisMM-3 trials to the entire trial cohort and found no new safety signals and similar overall response rates (8). Some real-world (RW) studies have shown that other MM treatments, such as thalidomide and bortezomib, have differing RW safety profiles between Western and Japanese or other East Asian populations (9–12). Other Pfizer-sponsored studies are being conducted that assess AE with elranatamab using real-world data (RWD), but these studies are all US-based and, thus far, similar RW evidence has not been generated in Japan.

As the first BCMA-directed bispecific monoclonal antibody approved in Japan, elranatamab represents a new addition to the treatment landscape for RRMM in Japan. This study aims to describe its RW use in clinical practice, including patterns of patient selection, treatment administration, and adverse event management in the post-approval setting. Utilizing a Japanese hospital-based administrative health dataset, which covers approximately 26% of all hospitals in Japan and includes over 40 million patient records, this study will describe the RW administration of elranatamab in patients with MM.

This noninterventional study is designated as a Post-Authorization Safety Study (PASS) and is conducted voluntarily by Pfizer.

8. RESEARCH QUESTIONS AND OBJECTIVES

Research Question: What are the characteristics of adult patients with MM who initiate elranatamab in Japan, and the SUD process, treatment patterns, HCRU, and safety associated with elranatamab administration?

The following objectives will be assessed among patients with MM receiving elranatamab:

Primary objectives:

- Objective 1: To describe patients with MM initiating elranatamab, including demographics, treatment and medical history.
- Objective 2: To describe and characterize elranatamab utilization, including timing, administration and dosing, during the follow-up period, including the step-up dosing (SUD) period.

Secondary objectives:

- Objective 3: To describe HCRU and costs associated with elranatamab usage during the follow-up period, including the SUD period.
- Objective 4: To describe the use of other treatments for MM including supportive therapy during the follow-up period.
- Objective 5: To describe incidence and prevalence of cytokine release syndrome (CRS), immune effector cell associated neurotoxicity syndrome (ICANS), and cytopenias during the SUD period.
- Objective 6: To describe infection incidence and prevalence during the follow-up period.

Exploratory objectives:

- Exploratory Objective 1: To describe the use of supportive medications during the SUD period and administration of IVIG within the 30-day post-index period.

9. RESEARCH METHODS

9.1. Study Design

This retrospective cohort study will assess the demographics, clinical history, SUD process, HCRU, and safety of elranatamab in MM patients with an elranatamab hospital claim. De-identified data from the Japan Medical Data Vision (MDV) will be used.

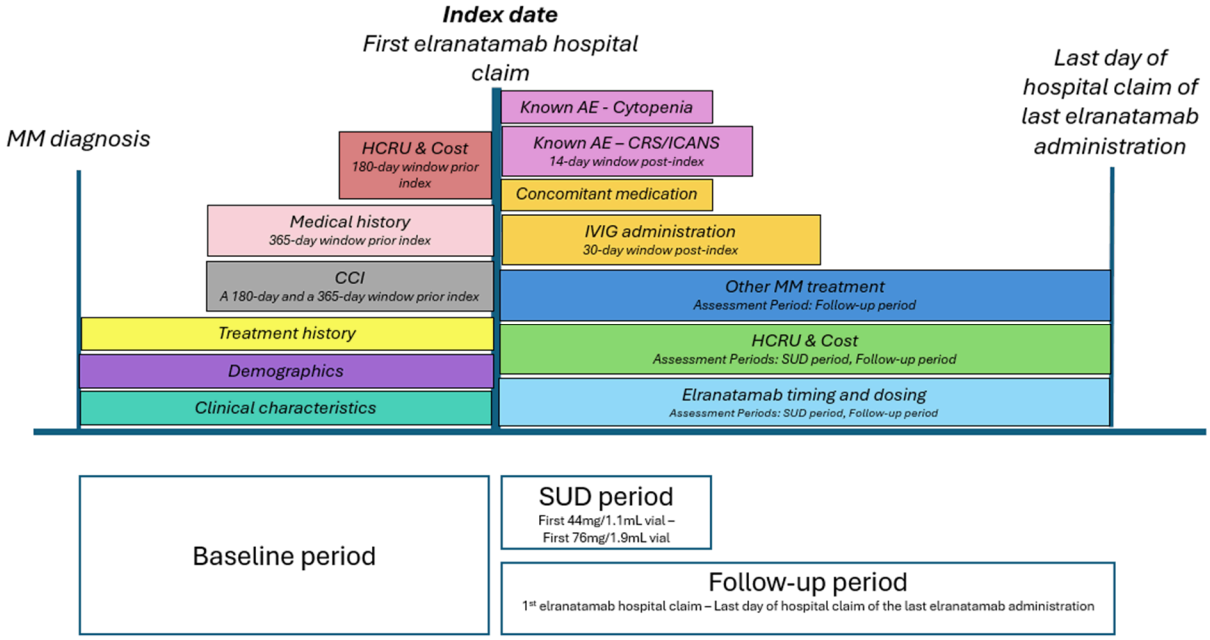
A retrospective cohort design was chosen because it allows for efficient use of existing RW data to evaluate treatment patterns and outcomes in a newly approved therapy, without the need for prospective data collection. This design is well-suited for descriptive analyses and enables timely insights into the early use of elranatamab in a RW setting.

The primary endpoints include patient demographics, clinical characteristics, and treatment patterns. Secondary endpoints include HCRU and safety outcomes. No formal measures of effect will be calculated. All analysis will be descriptive, with no a priori hypotheses or statistical comparisons between exposure groups.

The study population will be comprised of individuals aged 18 and older who initiated elranatamab between March 26, 2024, the PMDA approval date for elranatamab, and the end of data availability. The study period will be from the start of data availability, April 2008, to the end of data availability in MDV. The study period will remain the same for all study objectives. The patient baseline period will be from MM diagnosis to the start of the index treatment. The patient index date will be determined as the date of first hospital claim with an administration of elranatamab. The follow-up period will be defined as the period between the index date and the end of the hospital claim of the last elranatamab administration

inclusive. The SUD period will be defined as the period between the date of the first 44mg/1.1mL vial and the first 76mg/1.9mL vial of elranatamab, see more details in Section 9.2 and 9.3.1. Figure 1

Figure 1. Study design



Abbreviations:CCI: Charlson Comorbidity Index; HCRU: Health Care Resource Utilization; MM: multiple myeloma; SUD: Step-up dosing;

9.2. Setting

The study population will be extracted from MDV, a comprehensive resource based on hospital claims data and Diagnosis Procedure Combination (DPC) data. Information on demographics, mortality, laboratory tests, IP, OP, and ED claims, treatments, procedures, and costs are available for approximately 50 million patients. Patients will be identified using the inclusion and exclusion criteria listed in Sections 9.2.1 and 9.2.2. The inclusion and exclusion criteria ensure the study captures patients with MM who initiate elranatamab treatment in RW setting after its approval date in Japan. The exclusion criterion removes patients treated within clinical trials to avoid bias from controlled study conditions and ensure generalizability to routine clinical practice. These criteria may limit the number of eligible patients, especially early in the elranatamab post-approval period.

Index date: defined as the date of first hospital claim with elranatamab administration after March 26, 2024.

44mg/1.1mL vial of elranatamab: hospital claim of elranatamab with vial size of 44mg/1.1mL which corresponds to an SUD dose or a partial dose.

76mg/1.9mL vial of elranatamab: hospital claim of elranatamab with vial size of 76mg/1.9mL which corresponds to a full dose.

Study period: defined as the period between start of data availability to end of data availability in MDV.

Baseline period: defined as the variable period between MM diagnosis and first hospital claim of elranatamab administration (index date).

Medical history assessment window: defined as the 365-day window prior index date. If a patient has fewer than 365 days of data available prior to the index date, the assessment window will be equal to the maximum number of days available prior to the index date.

CCI assessment windows: defined as (1) the 180-day window prior index date and (2) the 365-day window prior to index date. If a patient has fewer than 180 days, or 365 days of data available prior to the index date, the assessment window will be equal to the maximum number of days available prior to the index date.

HCRU baseline assessment period: defined as the 180-day window prior index date. If a patient has fewer than 180 days of data available prior to the index date, the assessment window will be equal to the maximum number of days available prior to the index date.

SUD period: defined as the period between a patient's first 44mg/1.1mL vial of elranatamab and first 76mg/1.9mL vial of elranatamab, inclusive. See Section 9.3.1 and Annex 1 for more details. Within the SUD period, three sub-periods are identified:

- **Overall**: defined as the period between first 44mg/1.1mL vial and first 76mg/1.9mL vial of elranatamab.
- **First 44mg/1.1mL vial – Second 44mg/1.1mL vial**: defined as the period between the two 44mg/1.1mL vials of elranatamab, if second 44mg/1.1mL vial is administered.
- **Second 44mg/1.1mL vial – first 76mg/1.9mL vial**: defined as the period between the second 44mg/1.1mL vial and the first 76mg/1.9mL vial of elranatamab, if second 44mg/1.1mL vial is administered.

Follow-up period: defined as the period between the first hospital claim for elranatamab (index date) and the end of the hospital claim of the last elranatamab administration. Within this follow-up period, five sub-periods are identified (when sufficient follow-up time is available at the patient level). These sub-periods allow for reporting study endpoints across different phases of the follow-up period, and are based on expected dosing administrations and schedule of patients with switch to bi-weekly administrations from label guidance (see Table 10. Dosing Schedule of Elranatamab during Follow-up Period for Patients Switching to Q2W and Table 11. Dosing Schedule of Elranatamab during Follow-up Period for Patients staying on QW):

- **Index date to day 8:** defined as the first 8 days post-index date, inclusive. Also defined as day 1 to day 8.
- **Day 9 to day 168:** defined as the period from day 9 to day 168 post-index date.
- **Day 169+:** defined as the period from day 169 post-index date to end of follow-up period.

- **Overall follow-up:** defined as the period from index date to end of follow-up period.

IVIG follow-up assessment period: defined as the 30-day window post index date. If a patient has fewer than 30 days of data available post to the index date, the assessment window will be equal to the maximum number of days available post to the index date.

CRS/ICANS follow-up assessment period: defined as the 14-day window post index date. If a patient has fewer than 14 days of data available post to the index date, the assessment window will be equal to the maximum number of days available post to the index date.

9.2.1. Inclusion Criteria

Patients must meet all of the following inclusion criteria to be eligible for inclusion in the study:

1. First hospital health claim with an administration of elranatamab on or after March 26, 2024.
2. Have a diagnosis of MM.
3. Aged ≥18 years at the time of first hospital claim for elranatamab (i.e., index date).

9.2.2. Exclusion Criteria

Patients meeting any of the following criteria will not be included in the study:

1. Evidence of administration of elranatamab as part of a clinical trial.

9.3. Variables

This section outlines patient exposure groups, variable definitions, and study endpoints to be reported across all study objectives. All codes for variable identification will be provided in the statistical analysis plan (SAP). The data source for all variables is Japan MDV.

9.3.1 Exposure Groups and Assessment Periods

Table 1 outlines the variables to define exposure groups that will be used to identify patients and stratify analyses.

Table 1. Variables for Exposure

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
Study population	Exposure	MDV	All patients with MM who have a hospital claim for elranatamab after March 26, 2024, and who meet the inclusion and exclusion criteria outlined in Sections 9.2.1 and 9.2.2.	Index date
SUD Exposure Group	Exposure	MDV	Group A: Complete and timely SUD period Patients in the study population with two 44mg/1.1mL vials (second 44mg/1.1mL vial is received 1 to 7 days after the first) and one subsequent 76mg/1.9mL vial between 1 to 7 days after second 44mg/1.1mL vial Group B: Complete but not timely SUD period Patients in the study population with two 44mg/1.1mL vials and one subsequent 76mg/1.9mL vial after the second 44mg/1.1mL vial, with one or both intervals between doses ranging from 8 to 14 days. Group C: Alternative SUD period • Only one 44mg/1.1mL vial: patients in the study population with only one 44mg/1.1mL vial prior to receiving a 76mg/1.9mL vial • More than two 44mg/1.1mL vials: patients in the study population with more than	SUD period

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
			two 44mg/1.1mL vials prior to receiving a 76mg/1.9mL vial • Extremely untimely: patients in the study population with more than 14 days between the first and second 44mg/1.1mL vial or between the second 44mg/1.1mL vial and the first 76mg/1.9mL vial Note that patients who received only 44mg/1.1mL vials or only 76mg/1.9mL vials are not classified under any SUD exposure group but will remain part of the study population.	

Figure 2 illustrates possible elranatamab administration scenarios for each SUD group. These examples are not exhaustive and do not represent all potential administration schedules.

Figure 2. SUD Periods Administration Schedule

Table 2 summarizes the patient exposure groups and assessment periods during which endpoints for each study objective will be measured. Patients will be included in the follow-up sub-period analyses if they have at least one claim for elranatamab or if the end date of their follow-up period falls within the sub-period's time frame.

Table 2. Patient Exposure Groups Stratification and Assessment Period for Study Objectives

Study Objective	Assessment period	Patient Exposure Groups
Objective 1 – Patient Characteristics	Baseline period Index date	Study population Group A, Group A+B, Group C
Objective 2 – Treatment administration, dosing and timing	SUD period • Overall (Between first 44mg/1.1mL vial – first 76mg/1.9mL vial) • Between first 44mg/1.1mL vial – second 44mg/1.1mL vial • Between second 44mg/1.1mL vial – first 76mg/1.9mL vial	Group A, Group A+B, Group C
	Follow-up period • Index date	Study population

Study Objective	Assessment period	Patient Exposure Groups
	• Index date (day 1) to day 8 • Day 9 to day 168 • Day 169 to end of follow-up period • Overall (day 1 to end of follow-up period)	
Objective 3 – HCRU and costs	HCRU baseline assessment period	Study population
	SUD period • Overall (Between first 44mg/1.1mL vial – first 76mg/1.9mL vial) • Between first 44mg/1.1mL vial – second 44mg/1.1mL vial • Between second 44mg/1.1mL vial – first 76mg/1.9mL vial	Group A, Group A+B, Group C
	Follow-up period • Index date • Index date (day 1) to day 8 • Day 9 to day 168 • Day 169 to end of follow-up period • Overall (day 1 to end of follow-up period)	Study population
Objective 4 – Other MM treatments including supportive therapy	Follow-up period • Index date • Index date (day 1) to day 8 • Day 9 to day 168 • Day 169 to end of follow-up period • Overall (day 1 to end of follow-up period)	Study population
Objective 5 – Known adverse events	CRS/ICANS follow-up assessment period (CRS/ICANS events)	Group A, Group A+B, Group C
	SUD period (Cytopenia events) • Overall (Between first 44mg/1.1mL vial – first 76mg/1.9mL vial)	Group A, Group A+B, Group C

Study Objective	Assessment period	Patient Exposure Groups
	• Between first 44mg/1.1mL vial – second 44mg/1.1mL vial • Between second 44mg/1.1mL vial – first 76mg/1.9mL vial	
Objective 6 – Infections	Follow-up period • Index date • Index date (day 1) to day 8 • Day 9 to day 168 • Day 169 to end of follow-up period • Overall (day 1 to end of follow-up period)	Study population
Exploratory Objective 1 – Supportive medications	SUD period • Overall (Between first 44mg/1.1mL vial – first 76mg/1.9mL vial) • Between first 44mg/1.1mL vial – second 44mg/1.1mL vial • Between second 44mg/1.1mL vial – first 76mg/1.9mL vial	Group A, Group A+B, Group C
	IVIG follow-up assessment period	Group A, Group A+B, Group C

1.1.2. Covariates and Outcomes

Table 3 to Table 9 includes definitions and assessment periods for all study variables and that will be used to address the study objectives. Variables for which summary statistics across individuals are produced are identified in the table below. If applicable, the frequency and percentage of patients with missing data for each variable will be described.

Table 3. Variables for Baseline Characteristics (Objective 1 – Patient Characteristics)

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period
Age	Baseline characteristics	MDV	Age at index date, in years. Age will be reported as a continuous variable as well as a categorical variable for the following age groups: • <65 • 65-69 • 70-74 • ≥75	Index date
Sex	Baseline characteristics	MDV	Sex, N (%) • Male • Female	Index date
Weight	Baseline characteristics Sub-group identifier	MDV	Weight assessment before and closest to the index date, lb	Baseline period
Height	Baseline characteristics	MDV	Height assessment before and closest to the index date, cm	Baseline period
Smoking index	Baseline characteristics	MDV	Smoking index assessment before and closest to the index date Smoking index = Number of cigarettes smoked * years of smoking	Baseline period
Care setting	Baseline characteristics	MDV	Care setting for the first elranatamab administration • Inpatient (IP) • Outpatient (OP)	Index date

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period
Hospital scale	Baseline characteristics	MDV	Number of hospital beds in hospital admitted at index date (categorical) • ≤199 beds • 200-499 beds • ≥500 beds	Index date
Hospital category	Baseline characteristics	MDV	Hospital category at index date (categorical) • University hospital • Public hospital (local) • Public hospital (National) • Private hospital	Index date
CCI • Myocardial infarction • Congestive heart failure • Peripheral vascular failure • Cerebrovascular disease • Dementia • Chronic pulmonary disease • Rheumatic disease • Peptic ulcer disease • Mild liver disease • Severe liver disease • Diabetes w/o chronic complication • Diabetes with chronic complication • Mild renal disease	Baseline characteristics	MDV	Health claim code for comorbidities. CCI score using Glasheen algorithm (13) will be reported (continuous and categorical): • 0 to 1 • 2 to 5 • 6 to 9 • ≥ 10 Health claim code for each comorbidity will be reported.	180 days prior to index date 365 days prior to index date

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period
• Severe renal disease • Hemiplegia or paraplegia • Human immunodeficiency virus • AIDS • Metastatic solid tumor • Malignancy				
Activities of Daily Living (ADL) score	Baseline characteristics	MDV	ADL Score assessment before and closest to index date (categorical)	Baseline period
Hypercalcemia	Baseline characteristics	MDV	Disease code for hypercalcemia (Yes/No)	Baseline period
Hepatotoxicity	Baseline characteristics	MDV	Disease code for hepatotoxicity (Yes/No)	Baseline period
Renal failure	Baseline characteristics	MDV	Disease code for renal failure (Yes/No)	Baseline period
Amyloidosis	Baseline characteristics	MDV	Disease code for amyloidosis (Yes/No)	Baseline period
Hypertension	Baseline characteristics	MDV	Disease code for hypertension (Yes/No)	Baseline period
Plasmacytoma	Baseline characteristics	MDV	Disease code for plasmacytoma (Yes/No)	Baseline period
Extramedullary disease	Baseline characteristics	MDV	Disease code for extramedullary disease (Yes/No)	Baseline period

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period
Other hematological malignancies	Baseline characteristics	MDV	Disease code for hematological malignancies other than MM (Yes/No)	Baseline period
Any non-hematological malignancy	Baseline characteristics	MDV	Disease code for non-hematological malignancies (Yes/No)	Baseline period
Plasma cell leukemia	Baseline characteristics	MDV	Disease code for plasma cell leukemia (Yes/No)	Baseline period
Bone lesion	Baseline characteristics	MDV	Disease code for bone lesions (Yes/No)	Baseline period
Peripheral neuropathy	Baseline characteristics	MDV	Disease code for peripheral neuropathy (Yes/No)	Baseline period
Time since MM diagnosis	Baseline characteristics	MDV	Time (in months) from initial MM diagnosis to index date (continuous)	Baseline period
PIs	Baseline characteristics	MDV	Health claim code for bortezomib, carfilzomib, or ixazomib (Yes/No) Health claim code for each PI will also be reported.	Baseline period
IMiDs	Baseline characteristics	MDV	Health claim code for lenalidomide, thalidomide, or pomalidomide (Yes/No) Health claim code for each IMiD will also be reported.	Baseline period
anti-CD38s	Baseline characteristics	MDV	Health claim code for daratumumab, or isatuximab (Yes/No)	Baseline period

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period
			Health claim code for each anti-CD38 will also be reported.	
Penta-drug exposed	Baseline characteristics	MDV	Health claim code for all of the following therapies (Yes/No): • ≥2 distinct PIs (see generic names above • ≥2 distinct IMiDs (see generic names above) • ≥1 CD38 mAbs (generic names above)	Baseline period
Stem-cell transplant (SCT)	Baseline characteristics	MDV	Health claim code for SCT (Yes/No) Health claim code for each SCT type (allogeneic and autologous) will be reported.	Baseline period
CAR-T	Baseline characteristics	MDV	Health claim code for idecabtagene vicleucel or ciltacabtagene autoleucel (Yes/No) Health claim code for each CAR-T will be reported.	Baseline period
Chemotherapies	Baseline characteristics	MDV	Health claim code for chemotherapies (doxorubicin hydrochloride, melphalan, bendamustine, cyclophosphamide, etoposide, or cisplatin) (Yes/No) Health claim code for each chemotherapy will also be reported.	Baseline period
Intravenous immunoglobulin (IVIG)	Baseline characteristics	MDV	Health claim code for IVIG (Yes/No)	Baseline period

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period
Antibiotics	Baseline characteristics	MDV	Health claim code for antibiotic medications (Yes/No)	14 days prior index date 365 days prior index date
Antivirals	Baseline characteristics	MDV	Health claim code for antiviral medications (Yes/No)	14 days prior index date 365 days prior index date
Antifungals	Baseline characteristics	MDV	Health claim code for antifungal medications (Yes/No)	14 days prior index date 365 days prior index date

Abbreviations: ADL: Activity of Daily Living; CAR-T: chimeric antigen receptor T-cell therapy; CCI: Charlson Comorbidity Index; cm: centimeter; IMiDs: immunomodulatory agents; IP: inpatient; IVIG: intravenous immunoglobulin; lb: pound; OP: outpatient; PI: proteasome inhibitors; SCT: stem cell transplant.

Table 4. Variables for Outcomes (Objective 2 - Treatment Administration, Dosing and Timing)

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
44mg/1.1mL vial and 76mg/1.9mL vial [Summary statistic]	Outcome	MDV	Number of health claims for elranatamab per patient in the following categories: • 44mg/1.1mL vial • 76mg/1.9mL vial	SUD period

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
			Total number of health claims for elranatamab in the following categories: • 44mg/1.1mL vial • 76mg/1.9mL vial	Follow-up period
Time between first and second 44mg/1.1mL vials	Outcome	MDV	Days between claims for the first and second 44mg/1.1mL vial of elranatamab (continuous) Patients with <2 44mg/1.1mL vials are not included.	SUD period
Time between first 44mg/1.1mL vial and first 76mg/1.9mL vial	Outcome	MDV	Days between claims for the first 44mg/1.1mL vial and first 76mg/1.9mL vial of elranatamab (continuous)	SUD period
Time between second 44mg/1.1mL vial and first 76mg/1.9mL vial	Outcome	MDV	Days between claims for the second 44mg/1.1mL vial and first 76mg/1.9mL vial of elranatamab (continuous) Patients with <2 44mg/1.1mL vials are not included	SUD period
Time between elranatamab claims, patient level	Outcome	MDV	For patients with at least 2 elranatamab claims, the mean number of days between claims for elranatamab per patient will be reported	Follow-up period
Time between elranatamab claims, claim level	Outcome	MDV	For patients with at least 2 elranatamab claims, the mean number of days between claims for elranatamab will be reported alongside the number of intervals	Follow-up period

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
			between administrations in a given time period.	
Duration of treatment, patient level	Outcome	MDV	Days between first and last treatment administration for elranatamab (continuous)	Follow-up period
Duration of treatment, claim level	Outcome	MDV	Total calendar duration of elranatamb observation in days, and the date of the first observed elrantatamab claim	Follow-up period
Only 44mg/1.1mL vials [Summary statistic]	Outcome	MDV	Number of patients with only 44mg/1.1mL vials during the time period (yes/no)	Follow-up period
Only 76mg/1.9mL vials [Summary statistic]	Outcome	MDV	Number of patients with only 76mg/1.9mL vials during the time period (yes/no)	Follow-up period
Relative Administration Intensity (RAI) [Summary statistic]	Outcome	MDV	Ratio of the elranatamab administrations received divided by the expected number of administrations according to the Japan elranatamab label See Section 9.7.4 for more details	Follow-up period

Abbreviations: mL: millilitre; mg: milligram; RAI: Relative Administration Intensity; SUD: step-up dosing.

Table 5. Variables for Outcomes (Objective 3 – HCRU and Costs)

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
IP claim [Summary statistic]	Outcome	MDV	Number of patients with ≥1 all-cause IP claim (yes/no)	HCRU baseline period SUD period Follow-up period (overall only)
			Number of all-cause IP claims PPPM. Reported for all patients and for patients with ≥1 all-cause IP claim.	HCRU baseline period Follow-up period (overall only)
			Number of all-cause IP claims PPPD. Reported for all patients and for patients with ≥1 all-cause IP claim.	SUD period
OP claim [Summary statistic]	Outcome	MDV	Number of patients with ≥1 all-cause OP claim (yes/no)	HCRU baseline period SUD period Follow-up period (overall only)
			Number of all-cause OP claims PPPM. Reported for all patients and for patients with ≥1 all-cause OP claim.	HCRU baseline period Follow-up period (overall only)
			Number of all-cause OP claims PPPD. Reported for all patients and for patients with ≥1 all-cause OP claim.	SUD period

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
ED claim [Summary statistic]	Outcome	MDV	Number of patients with ≥1 all-cause ED claim (yes/no)	HCRU baseline period SUD period Follow-up period (overall only)
			Number of all-cause ED claims PPPM. Reported for all patients and for patients with ≥1 all-cause ED claim.	HCRU baseline period Follow-up period (overall only)
			Number of all-cause ED claims PPPD. Reported for all patients and for patients with ≥1 all-cause ED claim.	SUD period
Any HCRU (IP, OP, and ED) claim [Summary statistic]	Outcome	MDV	Number of patients with ≥1 all-cause HCRU (IP, OP, and ED) claim (yes/no)	HCRU baseline period SUD period Follow-up period (overall only)
			Number of all-cause HCRU claims PPPM. Reported for all patients and for patients with ≥1 all-cause HCRU claim.	HCRU baseline period Follow-up period (overall only)
			Number of all-cause HCRU claims PPPD.	SUD period

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
			Reported for all patients and for patients with ≥1 all-cause HCRU claim.	
Cost of IP claims [Summary statistic]	Outcome	MDV	Total cost of IP claims PPPM	HCRU baseline period Follow-up period (overall only)
			Total cost of IP claims PPPD	SUD period
Cost of OP claims [Summary statistic]	Outcome	MDV	Total cost of OP claims PPPM	HCRU baseline period Follow-up period (overall only)
			Total cost of OP claims PPPD	SUD period
Cost of ED claims [Summary statistic]	Outcome	MDV	Total cost of ED claims PPPM	HCRU baseline period Follow-up period (overall only)
			Total cost of ED claims PPPD	SUD period
Cost of HCRU claims [Summary statistic]	Outcome	MDV	Total cost of all-cause HCRU claims PPPM	HCRU baseline period Follow-up period (overall only)

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
			Total cost of all-cause HCRU claims PPPD	SUD period
Total duration of all-cause IP claims	Outcome	MDV	The total time in days of IP stays among patients who have at least 1 IP stay (continuous).	HCRU baseline period Follow-up period
Duration of all-cause IP claims	Outcome	MDV	Days of IP stays among patients who have at least 1 IP stay PPPM	HCRU baseline period Follow-up period
Department visits claims [Summary statistic]	Outcome	MDV	Number of patients with top 5 most common department visits claims (yes/no) Note that the top 5 will not be established a priori, but rather will be determined based on the data and sample	HCRU baseline period SUD period Follow-up period (overall only)
			Number of top 5 department visits claims PPPM Note that the top 5 will not be established a priori, but rather will be determined based on the data and sample	HCRU baseline period Follow-up period (overall only)
			Number of top 5 department visits claims PPPD Note that the top 5 will not be established a priori, but rather will be determined based on the data and sample	SUD period

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
Degree of nursing	Outcome	MDV	Highest degree of nursing recorded (categorical), N (%) For the following categories: No support, Support level 1, Support level 2, Care level 1, Care level 2, Care level 3, Care level 4, Care level 5, Is applying, Unknown	HCRU baseline period SUD period Follow-up period (overall only)

Abbreviations: ED: emergency department; HCRU: healthcare resource utilization; IP: inpatient; OP: outpatient; PPPD: per patient per day; PPPM: per patient per month; SUD: step-up dosing.

Table 6. Variables for Outcomes (Objective 4 - Other MM treatments including supportive therapy)

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
PIs	Outcome	MDV	Health claim code for bortezomib, carfilzomib, or ixazomib (Yes/No) Health claim code for each PI will also be reported.	Follow-up period
IMiDs	Outcome	MDV	Health claim code for lenalidomide, thalidomide, or pomalidomide (Yes/No) Health claim code for each IMiD will also be reported.	Follow-up period
anti-CD38s	Outcome	MDV	Health claim code for daratumumab, or isatuximab (Yes/No)	Follow-up period

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
			Health claim code for each anti-CD38 will also be reported.	
SCT	Outcome	MDV	Health claim code for SCT (Yes/No) Health claim code for each SCT (allogeneic and autologous) will be reported.	Follow-up period
CAR-T	Outcome	MDV	Health claim code for idecabtagene vicleucel or ciltacabtagene autoleucel (Yes/No) Health claim code for each CAR-T will be reported.	Follow-up period
Chemotherapies	Outcome	MDV	Health claim code for chemotherapies (doxorubicin hydrochloride, melphalan, bendamustine, cyclophosphamide, etoposide, or cisplatin) (Yes/No) Health claim code for each chemotherapy will also be reported.	Follow-up period
IVIG	Outcome	MDV	Health claim code for IVIG (Yes/No)	Follow-up period

Abbreviations: CAR-T: chimeric antigen receptor T-cell therapy; IMiDs: immunomodulatory agents; IVIG: intravenous immunoglobulin; PI: proteasome inhibitors; SCT: stem cell transplant;

Table 7. Variables for Outcomes (Objective 5 – Known Adverse Events)

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
CRS events[1]	Outcome	MDV	Disease code for CRS (Yes/No)	CRS/ICANS follow-up

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
			(14)Incidence and prevalence will be reported, see Section 9.7.2 for additional details.	assessment period
Frequency of CRS events	Outcome	MDV	Total number of CRS events during the time period per patient (categorical) • 1 CRS event • 2 CRS events • 3 or more CRS events	CRS/ICANS follow-up assessment period
CRS Concomitant medications	Outcome	MDV	Disease code for concomitant medications (i.e., IV hydration) received on the same day as the CRS event (Yes/No)	CRS/ICANS follow-up assessment period
Length of stay for CRS events	Outcome	MDV	The total time in days of the CRS hospital stays among patients who have at least 1 CRS event (continuous).	CRS/ICANS follow-up assessment period
Days from index to first CRS event	Outcome	MDV	Time in days from index date to first CRS event (continuous)	CRS/ICANS follow-up assessment period
ICANS events[1]	Outcome	MDV	Disease code for ICANS (Yes/No) Incidence and prevalence will be reported, see Section 9.7.2 for additional details.	CRS/ICANS follow-up assessment period
Frequency of ICANS events	Outcome	MDV	Total number of ICANS events during the time period per patient (categorical) • 1 ICANS event • 2 ICANS events	CRS/ICANS follow-up assessment period

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
			• 3 or more ICANS events	
ICANS Concomitant medications	Outcome	MDV	Disease code for concomitant medications (i.e., IV hydration) received on the same day as the ICANS event (Yes/No)	CRS/ICANS follow-up assessment period
Length of stay for ICANS events	Outcome	MDV	The total time in days of the ICANS hospital stays among patients who have at least an IP stay with ≥1 ICANS event (continuous).	CRS/ICANS follow-up assessment period
Days from index to first ICANS event	Outcome	MDV	Time in days from index date to first ICANS event (continuous)	CRS/ICANS follow-up assessment period
Cytopenia occurrence[1]	Outcome	MDV	Disease code or labs value for cytopenias occurrences (Yes/No): • Anemia • Leukopenia • Lymphopenia • Neutropenia • Thrombocytopenia Number and proportion of patients with a health claim code for each cytopenia will also be reported. Incidence and prevalence will be reported, see Section 9.7.2 for additional details.	SUD period
Days from index to first cytopenia	Outcome	MDV	Time in days from index date to first cytopenia (continuous)	SUD period

Abbreviations: CRS: cytokine release syndrome; ICANS: Immune effector Cell Associated Neurotoxicity Syndrome; SUD: step-up dosing.

Notes:

1. *Variable will be measured as incident and prevalent. Incident cases have a 30-day washout period applied.*

Table 8. Variables for Outcomes (Objective 6 - Infections)

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
Infection occurences[1]	Outcome	MDV	Disease code for infections; the list of infections of interest will be outlined in the SAP (Yes/No)Incidence and prevalence will be reported, see Section 9.7.2 for additional details.	Follow-up period
Days from index to infection	Outcome	MDV	Time in days from index date to first infection (continuous)	Follow-up period
Days between infections	Outcome	MDV	Days between infection claims (continuous) For patients with ≥2 disease code for infections listed in the SAP during the time period	Follow-up period

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
Antibiotics	Outcome	MDV	Health claim code for antibiotic treatment (Yes/No)	Follow-up period
Antivirals	Outcome	MDV	Health claim code for antiviral treatment (Yes/No)	Follow-up period
Antifungals	Outcome	MDV	Health claim code for antifungal treatment (Yes/No)	Follow-up period

Notes:

1. *Variable will be measured as incident and prevalent. Incident cases have a 60-day washout period applied.*

Table 9. Variables for Outcomes (Exploratory Objective 1 – Supportive Medications)

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
Dexamethasone	Outcome	MDV	Health claim code for dexamethasone (Yes/No)	SUD period
Diphenhydramine	Outcome	MDV	Health claim code for diphenhydramine (Yes/No)	SUD period
Acetaminophen	Outcome	MDV	Health claim code for acetaminophen (Yes/No)	SUD period
Tocilizumab	Outcome	MDV	Health claim code for tocilizumab (Yes/No)	SUD period

Variable	Role	Data Source	Operational Definition	
			Definition	Assessment Period(s)
IVIG	Outcome	MDV	Health claim code for IVIG (Yes/No)	IVIG follow-up assessment period

Abbreviations: IVIG: intravenous immunoglobulin; SUD: step-up dosing.

9.4. Data Sources

This study will utilize the MDV database. The MDV database is a comprehensive resource containing administrative data from over 540 hospitals in Japan, based on hospital claims data and Diagnosis Procedure Combination (DPC) data. This dataset includes information on demographics; mortality; laboratory tests; inpatient (IP), outpatient (OP), and emergency department (ED) claims; treatments; procedures; and costs of approximately 50 million patients, with a significant proportion of these patients being over 65 years old. The MDV database captures approximately 30% of advanced treatment hospitals in Japan, with over one million health claims processed each month. Additionally, the database includes health claim data from all insurance types (Social, National, and Elderly Insurance), providing a comprehensive characterization of patients and treatment paradigms. The MDV database has been used extensively for use in RW evidence generation (14). Studies have used the MDV database to report on the safety of treatments (15), including the safety of dose schedules (16–18), and treatment patterns in oncology (19–21).

Data is available from April 2008 through the most recent data cut. The MDV database is fully de-identified and aggregated. No individual patient can be identified; therefore, informed consent is not required.

9.5. Study Size

The study sample will be identified from secondary data from Japanese hospitals that has already been collected. As the MDV database does not include all Japanese hospitals, the sample will be a convenience sample. The most recent data cut available from MDV will be used for the report. All patients who meet the inclusion/exclusion criteria defined in Section 9.2 will be included in the analyses.

This is a descriptive study with no a priori hypotheses; therefore, formal sample size calculations are not applicable. However, to provide an indication of the expected sample size, the February 2025 data cut, MDV included 128 patients that had at least one hospital claim for elranatamab.

9.6. Data Management

The MDV database, a comprehensive, hospital-based, service-level, all-payer claims database managed by the vendor Medical Data Vision Co., Ltd, will serve as the primary data source for this study. The MDV database includes data from over 540 hospitals and healthcare systems across Japan, encompassing both IP and OP services. It integrates health insurance claims from all insurance types

(i.e., Social, National, and Elderly Insurance), providing a comprehensive representative view of RW clinical practice and treatment patterns.

Data will be de-identified prior to transfer from the vendor and monthly updates are being transferred. Data cleaning, transformation, and statistical analyses will be conducted using SAS. Snowflake will be used for secure data storage and preprocessing.

9.7. Data Analysis

All analysis will be descriptive in nature and no formal statistical comparisons will be performed between groups. All characteristics and endpoints will be reported separately for each assessment period and patient exposure groups of interest as defined in Table 2. Patient Exposure Groups Stratification and Assessment Period for Study Objectives.

Raw data transferred by MDV will be reviewed for completeness, consistency and plausibility. Records with missing or implausible values (e.g., negative age, invalid dates) will be flagged and addressed according to predefined rules in the SAP. Duplicate records will be identified and removed. Variables will be derived and categorized as needed for analysis. Diagnosis and procedure codes will be mapped to standardized categories using the International Classification of Diseases, 10th revision (ICD-10) and Healthcare Common Procedure Coding System (HCPCS) classification systems. Missing data will be reported, and no imputation will be performed unless otherwise specified in the SAP.

Detailed methodology for summary and statistical analyses of data collected in this study will be documented in a SAP, which will be dated, filed, and maintained by the sponsor. The SAP may modify the plans outlined in the protocol; any major modifications of primary endpoint definitions or their analyses would be reflected in a protocol amendment.

9.7.1. Descriptive Analysis

Dichotomous and categorical variables will be summarized by the number and percentage of patients in each category. Continuous variables will be described using mean, standard deviation (SD), median, interquartile range (IQR), minimum, and maximum. If applicable, the frequency and percentage of patients with missing data for each variable will be described. For reporting conventions, mean, median, and SD will be rounded to 1 decimal place. Percentages will be rounded to 1 decimal place.

9.7.2. Incidence and prevalence calculations

The incidence of CRS, ICANS, and cytopenias will be determined by counting the number of new cases that arise within a specified time frame, divided by the population at risk during that period. An incident case is defined as a new occurrence of the condition following a 30-day washout period, during which no previous cases are considered. The prevalence of CRS, ICANS, and cytopenia will be calculated by counting the total number of cases (both new and existing) present in the population at a specific point in time, divided by the total population size.

Similarly, the incidence of infections will be calculated by counting the number of new cases that arise within a specified time frame, with a 60-day washout period applied to define new cases. The prevalence of infections will be calculated by counting the total number of infection cases present in the population at a specific point in time, divided by the total population size.

$$Incidence\ Rate = \frac{Number\ of\ new\ cases}{Population\ at\ risk} * Population\ size$$

$$Prevalence\ Rate = \frac{Number\ of\ cases}{Total\ population} * 100$$

9.7.3. Relative Administration Intensity

RAI will be calculated as the cumulative frequency of administration received over the expected number of administrations. Since response is needed to determine if switching to bi-weekly doses is appropriate and is not available in MDV, two schedule definitions will be used to estimate the expected number of administration to calculate RAI (Table 10. Dosing Schedule of Elranatamab during Follow-up Period for Patients Switching to

Q2W and Table 11. Dosing Schedule of Elranatamab during Follow-up Period for Patients staying on

QWTable 10. Dosing Schedule of Elranatamab during Follow-up Period for Patients Switching to

Q2W).

$$RAI = \frac{Number\ of\ administrations\ received}{Number\ of\ expected\ administrations\ during\ the\ time\ period}$$

a) Schedule 1[1]

Assumption that all patients switch to bi-weekly doses (Q2W) after day 169 post-index.

Table 10. Dosing Schedule of Elranatamab during Follow-up Period for Patients Switching to Q2W

Follow-up Sub-Periods	Expected Administrations	Vial Size
Index date - Day 8	3 administrations	2 x 44mg/1.1mL 1 x 76mg/1.9mL
Day 9 - Day 168	1 administration per week	76mg/1.9mL
Day 169 – End of follow-up	1 administration every two weeks	76mg/1.9mL

Notes:

[1] Adapted from dosing and administration guidance of the Japanese elranatamab label available at https://labeling.pfizer.com/ShowLabeling.aspx?id=20462

b) Schedule 2[1]

Assumption that all patients continue with weekly doses (QW) after day 169 post-index.

Table 11. Dosing Schedule of Elranatamab during Follow-up Period for Patients staying on QW

Follow-up Sub-Periods	Expected Administrations	Vial Size
Index date - Day 8	3 administrations	2 x 44mg/1.1mL 1 x 76mg/1.9mL
Day 9 – End of follow-up	1 administration per week	76mg/1.9mL

Notes:
[1] Adapted from dosing and administration guidance of the Japanese elranatamab label available at https://labeling.pfizer.com/ShowLabeling.aspx?id=20462

Treatment exposure will be assessed across the different follow-up periods. End of follow-up is defined as the end of the hospital claim of the last elranatamab administration inclusive.

9.7.4. Healthcare Resource Utilization and Costs

All-cause HCRU will be measured as the total number IP, OP, and ED that occurred over the follow-up period. Health claims will only be counted once per day to estimate visits. Additionally, the total length of IP stays will be reported among patients with at least one IP visit. Costs will be adjusted for inflation. More details will be provided in the SAP.

PPPM

PPPM standardizes HCRU and cost by calculating the average of a specific variable or a number of specific events (e.g., ED health claims, IP health claims) per month for each patient. In this study, PPPM will be used to report ED, IP and OP visits and cost for the HCRU baseline period and the follow-up period. To obtain PPPM, the following formula will be used for each patient:

$$PPPM = \frac{Total\ number\ of\ events\ during\ a\ specfied\ period}{Duration\ of\ the\ specified\ period\ (in\ months)}$$

PPPD

PPPD standardizes HCRU and cost by calculating the average of a specific variable or a number of specific events (e.g., ED health claims, IP health claims) per day for each patient. In this study, PPPD

will be used to report ED, IP and OP visits and cost for the SUD period. To obtain PPPD, the following formula will be used for each patient:

$$PPPD = \frac{Total\ number\ of\ events\ during\ a\ specfied\ period}{Duration\ of\ the\ specified\ period\ (in\ days)}$$

This calculation will allow meaningful comparisons across patients with varying assessment period lengths, by normalizing resources use to a monthly rate. Summary statistics (mean, median, min, max) will then be reported to understand average monthly cost and utilization patterns across patients.

9.7.5. Subgroup analyses

A subgroup analysis will be conducted for patients identified as having low body weight at index date. The threshold defining "low weight" will be specified in detail within the SAP, based on clinical guidance.

This subgroup analysis will replicate the primary objectives (Objective 1 and Objective 2), as well as secondary objectives 5 and 6, which focus on known adverse events and infections following elranatamab administration.

9.7.6. Sensitivity analyses

No sensitivity analysis will be conducted as a part of this analysis.

9.8. Quality Control

STATLOG will code measures for patient identification, and study endpoints based on codes and algorithms described in this protocol and corresponding SAP. This protocol will be strictly followed when conducting the analysis of this study. All cohorts developed, statistical analyses implemented, and tables completed will undergo quality control review by at least one additional analyst or scientist under the supervision of the Study Lead. The Study Lead will review all results tables and other final deliverables to confirm accuracy, logical flow, and appropriate format.

MDV collects and utilizes both personal data and anonymously processed information in strict compliance with the Act on the Protection of Personal Information, the EU's General Data Protection Regulation (GDPR), and other applicable legal frameworks. Recognizing the sensitive nature of medical data, particularly that of patients and healthcare institutions, MDV is committed to ensuring the confidentiality, integrity, and proper use of such information. To this end, MDV implements robust safety management practices, including appropriate technical and organizational security measures, to prevent unauthorized access, data breaches, loss, or alteration of personal information.

In addition to technical safeguards, MDV emphasizes the importance of human factors in data protection. The organization conducts regular training and development programs for its staff to reinforce awareness and adherence to privacy protocols. Furthermore, MDV exercises strict oversight over any third-party entities entrusted with personal data, ensuring that outsourced data management aligns with its stringent security standards. Through these comprehensive measures, MDV upholds a high-level information security management system and demonstrates its ongoing commitment to protecting personal information in the healthcare domain.

9.9. Limitations of the Research Methods

This study is subject to limitations, described below:

- The MDV database follows patients' medical journey through the same facility, not between facilities – as such there is visibility only on prior diagnoses received within the same facility. There may be a loss in data continuity due to hospital transfers, however, patients in Japan tend to be treated in the same centers therefore this may be minimal.

- Measures of MM disease severity, such as ISS stage, M-protein level, and cytogenetic risk are not available in MDV. This limits the extent to which patients' MM can be characterized.

- This study will use a secondary data source. Because of the secondary data source, common limitations apply to this study, including:

    - Data may not be complete or accurate due to potential errors in coding or record-keeping at the point of the healthcare provider.

    - Lags in data availability can lead to inaccuracies in timing of reported information. This can particularly impact estimates over short periods of time (e.g., HCRU on index date).

    - Missing data cannot confirm the absence of a condition or value in a patient's medical history; only that it was not documented.

    - The internal process of obtaining and cleaning data is not fully known by scientists using RW databases, as such the internal validity of RWD remains largely unknown to scientists working with the data (19). Although there are concerns about the validity of RWD, the MDV database still has been used for a large number of peer-reviewed publications (14).

    - The lack of granularity of certain variables can limit the research that can be done; for example, granularity of grade of infection is often not available.

    - Clinical trials have close monitoring and prospective data collection, which RWD lacks. This means that the description of AEs in RW patients is expected to be less precise. Additionally, estimates of incidence and prevalence of safety events are likely to be underestimated compared to clinical trials or prospective studies where timing of assessments can be controlled. However, RWD can be useful to describe incidences of AEs in a larger and more heterogenous samples (20).

- This study population consists Japanese patients treated with elranatamab in Japan; however, the data does not cover all patients in Japan. As such, results may not fully represent the broader experience of patients receiving elranatamab both within Japan and internationally.

9.10. Other Aspects

Not applicable

10. PROTECTION OF HUMAN SUBJECTS

10.1. Patient Information

This study involves data that exist in deidentified/anonymized structured format and contain no patient personal information.

10.2. Patient Consent

As this study involves deidentified/anonymized structured data, which according to applicable legal requirements do not contain data subject to privacy laws, obtaining informed consent from patients by Pfizer is not required.

10.3. Institutional Review Board (IRB)/ Ethics Committee (EC)

Approval from an institutional review board/independent ethics committee is not required for this study as only de-identified secondary data sources will be used. Therefore, this study is considered exempt from the requirements for "human subjects research".

10.4. Ethical Conduct of the Study

The study will be conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value, and rigor, and follow generally accepted research practices described in the Guidelines of Good Pharmacoepidemiology Practices (GPP) issued by the International Society for Pharmacoepidemiology (ISPE) (24), Good Practices for Outcomes Research issued by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) (25), International Ethical Guidelines for Epidemiological issued by the Council for International Organizations of Medical Sciences (CIOMS) (26).

11. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

This study involves data that exist as structured data by the time of study start. In these data sources, it is not possible to link (i.e., identify a potential association between) a particular product and medical event for any individual. Thus, the minimum criteria for reporting an adverse event (AE) (i.e., identifiable patient, identifiable reporter, a suspect product, and event) cannot be met.

12. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

For all publications relating to the study, Pfizer will comply with recognized ethical standards concerning publications and authorship, including Section II - "Ethical Considerations in the Conduct and Reporting of Research" of the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, http://www.icmje.org/index.html#authorship, established by the International Committee of Medical Journal Editors. For this study, both interim and final study reports are planned for external dissemination in a manuscript submitted to a peer-reviewed, scientific journal or in an abstract/presentation at a scientific conference or symposium in accordance with these standards.

In the event of any prohibition or restriction imposed (e.g., clinical hold) by an applicable competent authority in any area of the world, or if the investigator party responsible for collecting data from the

participant is aware of any new information which might influence the evaluation of the benefits and risks of a Pfizer product, Pfizer should be informed immediately.

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None

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SUD period

The following tableTable 12. SUD schedule of elranatamab implemented in the study SUD periods outlines the SUD schedule for elranatamab, specifying the time intervals between 44mg/1.1mL vials and the first 76mg/1.9mL vial for each SUD period. It categorizes patients into different groups based on the timing of their administrations.

Table 12. SUD schedule of elranatamab implemented in the study SUD periods

Dosing Schedule	Group	Time Period	Expected Administrations	Vial size
SUD period	Group A	1 – 7 days between the first and second 44mg/1.1mL vial AND 1 – 7 days between the second 44mg/1.1mL vial and first 76mg/1.9mL vial	3 administrations	2 x 44mg/1.1mL 1 x 76mg/1.9mL
	Group B	8 – 14 days between the first and second 44mg/1.1mL vial AND/OR 8 – 14 days between second 44mg/1.1mL vial and first 76mg/1.9mL vial	3 administrations	2 x 44mg/1.1mL 1 x 76mg/1.9mL
	Group C – Only 1 44mg/1.1mL vial	No time period requirement	2 administrations	1 x 44mg/1.1mL 1 x 76mg/1.9mL
	Group C – More than 2 44mg/1.1mL vials	No time period requirement	4+ administrations	≥3 x 44mg/1.1mL 1 x 76mg/1.9mL
	Group C – Extremely untimely	≥14 days between the first and second 44mg/1.1mL vial	3 administrations	2 x 44mg/1.1mL 1 x 76mg/1.9mL

		AND/OR ≥14 days between second 44mg/1.1mL vial and first 76mg/1.9mL vial		

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