POST AUTHORISATION SAFETY STUDY (PASS) INFORMATION

Title	**A Non-interventional, Post-authorization Safety Study of Patients with Relapsed or Refractory Mantle Cell Lymphoma to Further Investigate and Characterize the Association of Lenalidomide With Tumor Flare Reaction and High Tumor Burden**
Version Identifier of the Final Study Report	Version 1.0
Date of Last Version of the Final Study Report	14-Oct-2024
EU PAS Register Number	EUPAS23366
Active Substance	Lenalidomide (ATC code: L04AX04)
Medicinal Product	Revlimid®
Product Reference	EU/1/07/391/001-014
Procedure Number	EMEA/H/C/000717/II/79
Marketing Authorisation Holder	Bristol-Myers Squibb Pharma EEIG
Joint PASS	No
Research Question and Objectives	This study was designed as a retrospective non-interventional study of patients with relapsed or refractory (R/R) mantle cell lymphoma (MCL) to further investigate the following objectives: <u>Primary Objective</u> To quantify and characterise the event of tumour flare reaction (TFR) by tumour burden (assessed based on the last computed tomography (CT) scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting. <u>Secondary Objective</u> To quantify and characterise the proportion of early deaths (defined as deaths within 20 weeks of the initial administration of lenalidomide) by tumour burden in R/R MCL patients treated with lenalidomide in a real-world setting.

Countries of Study	The study was performed in Europe. Potential sites were identified where R/R MCL patients were treated with lenalidomide and where lenalidomide was reimbursed for this indication. Identification of sites was done through partnerships such as, but not limited to that with the European Mantle Cell Lymphoma Registry. Other sources including knowledge of, or experience with sites could also be used for site identification purposes. Identified sites were assessed for feasibility and invited to participate in the study.
Author	[redacted]

MARKETING AUTHORISATION HOLDER

Marketing Authorisation Holder (MAH)	[redacted]
MAH Contact Person	[redacted]

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1 ABSTRACT

Title

A Non-interventional, Post-authorization Safety Study of Patients with Relapsed or Refractory Mantle Cell Lymphoma to Further Investigate and Characterize the Association of Lenalidomide With Tumor Flare Reaction and High Tumor Burden

Rationale and Background

In the European Union (EU), the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion on 28-Jan-2016 for the use of lenalidomide in the treatment of adult patients with relapsed or refractory mantle cell lymphoma. The European Commission (EC) granted a marketing authorisation for this indication on 08-Jul-2016.

While the marketing authorisation was granted, the Pharmacovigilance Risk Assessment Committee (PRAC) review of the Risk Management Plan (RMP) led to a request for further assessment of safety issues via post marketing surveillance. This relapsed or refractory mantle cell lymphoma (R/R MCL) post-authorisation safety study (PASS) aimed to gather additional safety information as a multinational, non-interventional study (NIS) to further investigate the primary and secondary objectives described below.

Research Question and Objectives

This study was designed as a retrospective non-interventional study of patients with R/R MCL to further investigate the following objectives:

Primary Objective

- To quantify and characterise the event of tumour flare reaction (TFR) by tumour burden (assessed based on the last computed tomography [CT] scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting.

Secondary Objective

- To quantify and characterise the proportion of early deaths (defined as deaths within 20 weeks of the initial administration of lenalidomide) by tumour burden in R/R MCL patients treated with lenalidomide in a real-world setting.

Study Design

This was a European multinational, retrospective, non-interventional study of patients with R/R MCL.

Potential sites were identified where R/R MCL patients were treated with lenalidomide. Site inclusion was limited to countries where lenalidomide was reimbursed for this indication. Identification of sites was done through partnerships such as, but not limited to that with the European Mantle Cell Lymphoma Registry. Other sources including knowledge of, or experience with sites could also be used for site identification purposes. Identified sites were then assessed for feasibility and invited to participate in the study.

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All data were collected retrospectively from identified patients following the first dose of lenalidomide treatment for up to 6 months including those patients who died within this data collection period.

A common set of key variables in accordance with the study objectives was identified in the medical records of eligible MCL patients and was entered into an electronic case report form (eCRF).

Setting

The study population consisted of a retrospective cohort of R/R MCL patients who had commenced treatment with lenalidomide after 08-Jul-2016 (date marketing authorisation was granted).

Subjects and Study Size, Including Dropouts

Patients must have met the following inclusion/exclusion criteria to be eligible for the study:

Inclusion Criteria:

1) Received at least one dose of lenalidomide commencing after 08-Jul-2016 for the treatment of R/R MCL.
2) Informed consent of the patient or an authorised third person or authority, if required by law, given prior to data collection.
3) Patient was to be ≥18 years of age at the time of signing the informed consent form (ICF).

Exclusion Criteria:

1) Patients were to be excluded if they were participating in an interventional clinical trial during the treatment period under observation in this PASS.

Study Size:

Although the exact number of R/R MCL patients treated with lenalidomide in Europe was not known, internal data estimated the number of patients who receive second-line therapy in 5 countries of Europe (France, Germany, Italy, Spain and the United Kingdom) as 1,632 per year; and of those, 6% received lenalidomide alone or in combination with rituximab (Decision Resources Group internal data).

Additionally, an estimated 783 patients annually received ≥ third-line therapy, of which 11% were treated with lenalidomide alone or in combination with rituximab. The number of patients receiving lenalidomide for additional lines of therapy after third-line was expected to be very low. Based on these internal estimates, approximately 184 cases per year of R/R MCL patients potentially received second- or third-line lenalidomide treatment.

However, these estimates for treatment with lenalidomide are higher than published real-world data on treatment patterns for R/R MCL (2.3% to 2.7% usage of lenalidomide in second-line treatment).[1,2,3] Further limitations on the feasibility of recruiting patients included enrolling patients only in countries where lenalidomide was reimbursed, the introduction of new agents for R/R MCL, and a significant number of clinical trials for investigational agents in R/R MCL.

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Therefore, based on the above, recruitment of a fixed number of 100 patients was considered feasible within the estimated study selection period.

Estimation of the Cumulative Incidence of TFR

The calculation of precision for the cumulative incidence of TFR was based upon the observed cumulative incidence of TFR (9.6%) in the CC-5013-MCL-002 study[4] of 167 R/R MCL patients treated with lenalidomide with an exact two-sided 95% confidence interval (CI) = (5.6%; 15.1%). From the CC-5013-MCL-002 study, there was a 20% chance that the cumulative incidence of TFR would exceed 12.0% (upper limit of the one-sided 80% CI). Under the assumption of a true TFR cumulative incidence rate of 9.6%, the precision on the estimate of the TFR cumulative incidence rate with 100 patients was 7.5% (upper limit of the exact two-sided 95% CI). Under the assumption of a true TFR cumulative incidence rate of 12% in the study population, the precision on the estimate of the TFR cumulative incidence rate with 100 patients was 8.0% (upper limit of the exact two-sided 95% CI).

Estimation of Early Death Rate

In Study CC-5013-MCL-002, 13.2% (22/167) of lenalidomide-treated patients died early (within 20 weeks from the first dose of lenalidomide). The exact two-sided 95% CI was (8.4%; 19.3%), and there was only a 20% chance that the early death rate would exceed 15.9% (upper limit of the one-sided 80% CI). With 100 patients, the study allowed a calculation of the early death rate with a precision of +8.2% for the upper limit of the exact two-sided 95% CI for an observed rate of 13.2%, and +8.7% for an observed rate of 15.9%.

Variables and Data Sources

Variables:

Variables to be evaluated in this study included baseline demographic and clinical variables (the "population dataset"), treatment variables related to lenalidomide use and other relevant medications (the "treatment dataset"), and the outcome variables for safety (the "outcomes dataset").

Data Sources:

Data from individual patient medical charts were used as source data. The treating physician or an authorised delegate was to enter the data from these charts into the web-based eCRF. Data entry for each enrolled patient was only to start at least 6 months after the first dose of lenalidomide.

Results

Analyses reflect patient data collected between 02-Oct-2018 (first patient enrolled) through 10-Jan-2024 (last patient last visit). Database lock was 20-Feb-2024.

A total of 105 patients were screened. Among these, 103 patients (98.1%) received at least one dose of treatment and were included in the Safety Analysis Set (SAS) and, 101 (96.2%) met the eligibility criteria to comprise the Per Protocol Analysis Set (PPAS).

In the PPAS, the median age was 74.0 years (min: 44, max: 91) and 79.2% of patients were male.

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The median time from initial MCL diagnosis to start of lenalidomide was 51 months (min: 2, max: 207). The median lenalidomide treatment duration was 22.0 weeks (min: 0.4, max: 28.4) with a median cumulative dose of lenalidomide of 1340.00 mg (min: 20.0, max: 3800.0).

At baseline, low tumour burden was reported in 48 patients (47.5%) and high tumour burden in 15 patients (14.9%). Tumour burden was not documented in the medical charts for 38 patients (37.6%)

Primary Objectives

In the PPAS, the cumulative incidence, ie, incidence proportion, of TFR was 5.9% (95% CI: 2.2%, 12.5%) over the study period and the incidence rate of TFR was 14.4 per 100 person-years (PY; 95% CI: 6.5, 32.1). The cumulative incidence of TFR was numerically greater in patients with high tumour burden at baseline than in patients with low tumour burden at baseline (13.3% [95% CI: 1.7%, 40.5%] vs. 2.1% [95% CI: 0.1%, 11.1%], respectively). Similarly, the incidence rate of TFR was numerically greater in patients with high tumour burden at baseline than in patients with low tumour burden at baseline (34.2 per 100 PY [95% CI: 8.5, 136.6]) vs. 4.7 per 100 PY [95% CI: 0.7, 33.3], respectively), though the 95% CIs were wide. Among patients with unknown tumour burden at baseline, the cumulative incidence of TFR was 7.9% (95% CI: 1.7%, 21.4%) and the incidence rate of TFR was 20.9 per 100 PY (95% CI: 6.7, 64.7).

Secondary Objectives

In the PPAS, the cumulative incidence of early death was 19.8% (95% CI: 12.5%, 28.9%) and the incidence rate of early death was 57.8 per 100 PY (95% CI: 37.3, 89.6). The cumulative incidence of early death was numerically greater in patients with high tumour burden at baseline than in patients with low tumour burden at baseline (20.0% [95% CI: 4.3%, 48.1%] vs. 12.5% [95% CI: 4.7%, 25.2%]). The incidence rate of early death was also numerically greater in patients with high tumour burden at baseline than in patients with low tumour burden at baseline (61.5 per 100 PY [95% CI: 19.8, 190.7] vs. 34.9 per 100 PY [95% CI: 15.7, 77.7]), though the 95% CIs were wide. Among patients with unknown tumour burden at baseline, the cumulative incidence of early death was 28.9% (95% CI: 15.4%, 45.9%) and the incidence rate of early death was 87.6 per 100 PY (95% CI: 48.5, 158.2).

Other Safety Results

Only treatment-emergent adverse events (TEAEs) related to lenalidomide that were not reported in the current Revlimid EU Summary of Product Characteristics (SmPC; "related adverse events [AEs]") were reported in this study.

Related AEs reported in the SAS were the same as those reported in the PPAS.

In the PPAS, related AEs were reported in 10 patients (9.9%) and related serious adverse events (SAEs) in 4 patients (4.0%). Related SAEs consisted of death, encephalopathy, general physical health deterioration, immune thrombocytopenia, and venoocclusive liver disease. Related AEs leading to death were reported in 3 patients (3.0%) and consisted of death, general physical health deterioration, and venoocclusive liver disease. Related AEs leading to permanent lenalidomide

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discontinuation were reported in 2 patients (2.0%) and consisted of graft versus host disease in gastrointestinal tract and haemophagocytic lymphohistiocytosis.

No pregnancy data was collected as part of this retrospective study.

Discussion

Study CC-5013-MCL-005 was conducted to further characterise potential safety events of TFR and early deaths by tumour burden, as well as other potential safety risks, in R/R MCL patients in a real-world setting.

In total, 101 patients received lenalidomide and met the eligibility criteria for the PPAS.

The cumulative incidence of TFR was 5.9% overall, 13.3% in patients with high tumour burden at baseline and 2.1% in patients with low tumour burden at baseline.

Overall, the proportion of patients in this study who experienced TFR was lower than that observed previously in clinical trials. In study MCL-002, 9.6% of lenalidomide-treated subjects (16/167) experienced TFR. Of these 16 subjects, 3 (1.8%) experienced Grade 3 or 4 TFR, including 1 subject (0.6%) who experienced serious TFR and 1 subject (0.6%) who experienced TFR resulting in treatment discontinuation. In study MCL-001 (EMERGE), 9.7% of lenalidomide-treated subjects (13/134) experienced TFR events (Grade 1 to 2). No subjects discontinued lenalidomide therapy due to TFR. In a Phase 2 study conducted in 38 subjects with MCL treated with lenalidomide in combination with rituximab and followed for 9 years, 14 subjects (36.8%) experienced TFR (4 subjects [10.5%] had Grade ≥3 TFR).

In this observational study, the cumulative incidence of early deaths was 20.0% (95% CI: 4.3%, 48.1%) in patients with high tumour burden at baseline, which was comparable with the results in clinical trial MCL-002 (19.8% [16/81]). In the overall study population, the cumulative incidence of early deaths in this observational study was 19.8% (95% CI: 12.5%, 28.9%) and was greater than that observed in clinical trial MCL-002 (13.2% [22/167] in lenalidomide-treated subjects).

Overall, this study shows that the cumulative incidence of TFR and the cumulative incidence of early death in R/R MCL patients treated with lenalidomide in a real-world setting were consistent with what had been previously reported in the MCL lenalidomide clinical trials.

This study also collected information about AEs related to lenalidomide that were not reported in the current Revlimid EU SmPC. Related AEs were reported in 10 patients (9.9%). Each related AE was reported in a single patient. Four (4) patients experienced related SAEs, including 3 patients who had related AEs leading to death (death, general physical health deterioration, and venoocclusive liver disease). Two (2) patients experienced related AEs leading to permanent lenalidomide discontinuation (graft versus host disease in gastrointestinal tract and haemophagocytic lymphohistiocytosis). The results of this study suggest that there are no new safety concerns associated with lenalidomide treatment in R/R MCL patients that were not previously identified as part of the clinical development program.

This final study report provides insight into the occurrence of TFR and early deaths in patients with R/R MCL treated with lenalidomide in a real-world clinical setting. During the study period,

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the incidence of TFR was 5.9% and the incidence of early death was 19.8%. In addition, despite the small MCL patient population, the results of this study suggest that patients with higher tumour burden at baseline have a higher risk of TFR compared with those whose tumour burden is lower at baseline. Thus, treating physicians may consider more closely monitoring those patients with higher tumour burden at baseline after initiating lenalidomide treatment, as recommended in the currently approved SmPC. Finally, no new safety concerns were identified in this study, which is aligned with the results of the previous trials; therefore, there are no changes required regarding safety concerns as reflected in the current RMP and SmPC.

Marketing Authorisation Holder

Bristol-Myers Squibb Pharma EEIG

Names and Affiliations of Principal Investigators

The list of investigators is provided in Appendix 1.4.

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2 LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse event
CHMP	Committee for Medicinal Products for Human Use
CI	Confidence interval
CLL	Chronic lymphocytic leukemia
CRO	Contract research organisation
CT	Computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
EC	European Commission
ECOG PS	Eastern Cooperative Oncology Group Performance Status
eCRF	Electronic case report form
EDC	Electronic data capture
EU	European Union
HR	Hazard ratio
ICF	Informed consent form
IEC	Independent Ethics Committee
IMiD®	IMiDs® are a proprietary series of drugs with immunomodulatory and other properties
IQR	Interquartile range
IR	Incidence rate
IRB	Institutional Review Board
KM	Kaplan-Meier
MAH	Marketing authorisation holder
MCL	Mantle cell lymphoma
MDS	Myelodysplastic syndrome
MedDRA	Medical dictionary for regulatory activities
MIPI	Mantle Cell Lymphoma International Prognostic Index
MM	Multiple myeloma
NHL	Non-Hodgkin’s lymphoma
NIS	Non-interventional study
OS	Overall survival

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Abbreviation	Definition
PASS	Post-authorisation safety study
PPAS	Per Protocol Analysis Set
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic Safety Update Report
PT	Preferred term
PY	Person-year
RMP	Risk Management Plan
R/R	Relapsed or refractory
SAE	Serious adverse event
SAP	Statistical analysis plan
SAS	Safety Analysis Set
SmPC	Summary of Product Characteristics
SOC	System Organ Class
TEAE	Treatment-emergent adverse event
TFR	Tumour flare reaction
US	United States
WHO	World Health Organisation

3 INVESTIGATORS

The list of investigators is provided in Appendix 1.4.

4 OTHER RESPONSIBLE PARTIES

Study contact information is provided in Table 4-1.

Table 4-1: Contact Information

Sponsor:	[redacted]
Contract Research Organisation (CRO):	[redacted]

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Table 4-1: Contact Information

CRO Study Manager:	[redacted]
Celgene Global Trial Manager:	[redacted]
Celgene Physician:	[redacted]

5 MILESTONES

Milestones for this study are summarised in Table 5-1.

Analyses reflect data collected from 02-Oct-2018 (first patient enrolled) to 10-Jan-2024 (last patient last visit). The database was locked on 20-Feb-2024.

Table 5-1: Milestones

Milestone	Planned Date	Actual Date
Start of Data Collection	Q1 2019	02-Oct-2018
End of Patient Recruitment		10-Jan-2024*
End of Data Collection	Q4 2023	10-Jan-2024*
Registration in the EU PAS Register	03-May-2018	03-May-2018
First Independent Ethics Committee (IEC)/Institutional Review Board (IRB) approval	NA	
Initial Protocol (Version 3.0)		27-Aug-2018
Protocol Amendment (Version 4.0)		10-Nov-2020
Protocol Amendment (Version 5.0)		01-Dec-2023
Last IEC/IRB Approval	NA	
Initial Protocol (Version 3.0)		11-Jul-2019
Protocol Amendment (Version 4.0)		01-Feb-2021
Protocol Amendment (Version 5.0)		08-Apr-2024
Study Progress Report:		
Risk Management Plan (RMP)/Periodic Safety Update Reports (PSURs)	Annual as per PSUR cycle	Annual as per PSUR cycle
Final Report of Study Results	Q4 2024	Please reference the date on the signature page

*Although the targeted number of patients was reached in Q4 2023, an additional eligible patient was enrolled in January 2024.

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6 RATIONALE AND BACKGROUND

6.1 RATIONALE

Lenalidomide is a member of a proprietary series of drugs with immunomodulatory and other properties, referred to as IMiDs®[1].

In the United States (US), lenalidomide as monotherapy received regulatory approval on 05-Jun-2013, for the treatment of patients with mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib. In the European Union (EU), the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion on 28-Jan-2016 for the use of lenalidomide in the treatment of adult patients with relapsed or refractory mantle cell lymphoma. The European Commission (EC) granted a marketing authorisation for this indication on 08-Jul-2016.

While the marketing authorisation was granted, the Pharmacovigilance Risk Assessment Committee (PRAC), after reviewing the Risk Management Plan (RMP), requested further assessment of safety issues via post marketing surveillance. This relapsed or refractory (R/R) MCL post-authorisation safety study (PASS) aimed to gather additional safety information as a multinational, non-interventional study (NIS) to further investigate the research objectives described in Section 7.2.

6.2 BACKGROUND

Mantle cell lymphoma is a type of non-Hodgkin's lymphoma (NHL), currently defined as per the World Health Organisation Classification of Tumours of Haemaotopoietic and Lymphoid Tissues[5] with differing clinical features and responses to treatment.[6] The annual incidence of MCL in Europe was estimated as 0.45 cases per 100,000 persons based on cancer registry data from 20 countries.[7] Patients with MCL typically are predominantly male and Caucasian with a median age of > 60 years, and present with advanced stage disease. Despite intensive induction therapies in the front-line setting of young and fit patients, the clinical course is typically that of repeated relapses, and median survival of MCL is only 3 to 5 years.[8,9]

6.2.1 Study CC-5013-MCL-002

Study CC-5013-MCL-002 (SPRINT; hereinafter Study MCL-002), ClinicalTrials.gov number: NCT00875667, was the main study and basis for the marketing authorisation for the R/R MCL indication granted on 08-Jul-2016 by the EC.

Study MCL-002 was a randomised, Phase 2 study of patients with MCL aged 18 years or older at 67 clinics and academic centres in 12 countries who relapsed 1 to 2 times, had Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 to 2, at least 1 measurable lesion to be eligible, and who were ineligible for intensive chemotherapy or stem-cell transplantation.

Between 30-Apr-2009 and 07-Mar-2013, 254 patients were enrolled: 170 (67%) were randomly assigned to receive lenalidomide (Lenalidomide Arm), 84 (33%) to receive investigator's choice monotherapy (Control Arm). Patients had a median age of 68.5 years and received a median of

[1] IMiDs® are a proprietary series of drugs with immunomodulatory and other properties.

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2 previous regimens. With a median follow-up of 15.9 months, lenalidomide significantly improved progression-free survival compared with investigator's choice (median 8.7 months [95% confidence interval {CI}: 5.5, 12.1] vs. 5.2 months [95% CI: 3.7, 6.9]) with a hazard ratio (HR) of 0.61 (95% CI: 0.44, 0.84; p = 0·004). In the 167 patients in the Lenalidomide Arm and 83 patients in the Control Arm who received at least one dose of treatment, the most common Grade 3 or 4 adverse events (AEs), respectively, included neutropenia (73 [44%] vs. 28 [34%]) without increased risk of infection; thrombocytopenia (30 [18%] vs. 23 [28%]); leucopoenia (13 [8%] vs. 9 [11%]); and anaemia (14 [8%] vs. 6 [7%]).[4]

6.2.2 Tumour Flare Reaction in Study MCL-002

Tumour flare reaction (TFR) is an AE that is associated with treatment of patients with lymphoma or chronic lymphocytic leukaemia (CLL) with immunomodulatory drugs, but not chemotherapy, due to the specific mode of action of IMiDs.[10,11,12,13,14,15,16,17,18,19] It clinically presents with painful lymph nodes and/or spleen enlargement and can be accompanied by fever, rash, or lymphocytosis. TFR has been reported as a new important identified risk specific to lenalidomide treatment of CLL and B-cell lymphomas, but was not reported in association with the other target populations for Revlimid® (multiple myeloma [MM]; myelodysplastic syndrome [MDS]). TFR usually develops early in the course of therapy and may mimic progression of disease, and subsides and resolves over time. Symptomatic treatment is used depending on the severity of the TFR.

In study MCL-002, TFR was reported in the lenalidomide arm only (16 of 167 patients, [9.6%]) but not in the control arm (single-agent therapy with chemotherapy or rituximab). Of these 16 TFR events, the events in 3 (1.8%) subjects were classified as Grade 3 or 4 events (no Grade 5 AEs were reported): 1 event (0.6%) was a serious AE (SAE) (Celgene data on file) and 1 event (0.6%) resulted in treatment discontinuation. All TFR events occurred in Cycle 1 of treatment, except for 1 TFR event that started in Cycle 2. The median time to TFR was 1.1 weeks (interquartile range [IQR]: 0.7, 2.4).[4]

The variables that remained in the final multivariable model in Study MCL-002, which were strongly and independently correlated with TFR included high Mantle Cell Lymphoma International Prognostic Index (MIPI) score at diagnosis (p = 0.084) and bulky disease at baseline (p = 0.020).

In Study MCL-002, no SAEs of TFR were observed in the group of subjects with high absolute lymphocyte count (> 15 g/L) at baseline. Therefore, these subjects do not seem to be at a particularly high risk for such events, supporting the analyses for TFR in which an elevated site blood cell count at baseline was not an independent risk factor for the occurrence of TFR.

In the Revlimid Summary of Product Characteristics (SmPC), TFR has been listed as an adverse drug reaction (Revlimid SmPC Section 4.8),[20] added as a specific warning (Revlimid SmPC Section 4.4),[20] and cited as an important identified risk for the MCL and follicular lymphoma indications in the most current EU RMP (Version 40.1).

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6.2.3 Tumour Burden and Early Deaths in Study MCL-002

In study MCL-002, there was an overall risk reduction of 11% for overall survival (OS), a secondary endpoint, when comparing the lenalidomide arm to the control arm (HR of 0.89 [95% CI: 0.62, 1.28]; p = 0.519, log-rank test). However, there was also an increase in early deaths, defined as within 20 weeks of randomisation, in lenalidomide-treated patients (22/167 [13.2%]) in the lenalidomide arm vs. 6/83 (7.2%) patients treated in the control arm.

It is important to note that there was an imbalance in important baseline disease-related risk factors between treatment arms, which disfavoured subjects in the Lenalidomide Arm. This included high-risk MIPI scores, elevated levels of lactate dehydrogenase, bulky disease, and high tumour burden, all of which were more frequently observed in the Lenalidomide Arm. The proportion of patients with high tumour burden (defined by at least one lesion 5 cm or more in diameter or three lesions 3 cm or more in diameter by central radiology review) in the Lenalidomide Arm was 81 (48%) of 170 patients vs. 28 (33%) of 84 patients in the Control Arm (investigator's choice of monotherapy with either chlorambucil, cytarabine, rituximab, fludarabine, or gemcitabine).[4]

Additional analyses were done to further characterise these early deaths with respect to disease-related characteristics. Based on a multivariable analysis, only high tumour burden at baseline was identified as a significant risk factor for early death. Treatment was not identified as a risk factor in the multivariable analysis.

The proportion of subjects with high tumour burden at baseline who died within 20 weeks (19.8% vs. 7.1%) and within 52 weeks (39.5% vs. 21.4%) after randomisation was greater in the Lenalidomide Arm compared with the Control Arm (Celgene data on file).

In the lenalidomide arm, 11 (13.6%) of the 81 subjects who had high tumour burden at baseline discontinued treatment during Cycle 1 and the majority of these (7 of 11 subjects) did so due to treatment-emergent adverse events (TEAEs). In comparison, 4 (5.1%) of the 78 subjects who had low tumour burden at baseline discontinued treatment during Cycle 1; the majority of these (3 of 4 subjects) also discontinued treatment due to TEAEs (Celgene data on file).

In the control arm, 1 (3.6%) of the 28 subjects who had high tumour burden at baseline discontinued treatment during Cycle 1 (Celgene data on file).

Based on the above data, high tumour burden is a relevant factor for early death, regardless of treatment arm. However, it remains possible that the presence of TFR, an adverse event related to lenalidomide use, could have contributed to the early death in addition to high tumour burden. This hypothesis could not be tested given that there is no TFR case in the control group. It is unfortunate that in the MCL-002 study,[4] the protocol did not use tumour burden at baseline as a stratification factor.

7 RESEARCH QUESTION AND OBJECTIVES

7.1 RESEARCH QUESTION

This study was designed as a retrospective non-interventional study of patients with R/R MCL to further investigate the research objectives described in Section 7.2.

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7.2 RESEARCH OBJECTIVES

7.2.1 Primary Objective

To quantify and characterise the event of TFR by tumour burden (assessed based on the last computed tomography (CT) scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting.

7.2.2 Secondary Objective

To quantify and characterise the proportion of early deaths (defined as deaths within 20 weeks of initial administration of lenalidomide) by tumour burden in R/R MCL patients treated with lenalidomide in a real-world setting.

8 AMENDMENTS AND UPDATES

The initial protocol (Version 3.0 dated 27-Mar-2017) and the PRAC-endorsed protocol amendments are provided in Appendix 1.1.

Table 8-1: Amendments and Updates

Number	Date	Main Changes
Amendment 1 (Version 4.0)	16-Sep-2019	The purpose of this amendment was to make practical changes to the study data sources regarding the cohorts and site inclusion processes. There is now only one data source with standardised site selection, patient identification, and data management practices. Furthermore, additional clarification has been provided to ensure that data entry will start only 6 months after the first lenalidomide dose and regarding inclusion of patients who have died and cannot consent. Practical details such as key study personnel and MAH holder have also been updated. The statistical section has been modified to further specify analyses to be performed and to define baseline variables. Creatinine clearance has been included as a variable for analysis.
Amendment 2 (Version 5.0)	20-May-2022	The purpose of this amendment was to revise the study size and study milestones based on challenges with recruitment. Therefore, the Study Size section and Study Milestones were updated to reflect this change. Practical details, such as key study personnel, have also been updated. Clarification of the Common Terminology Criteria for Adverse Events versions has also been included.

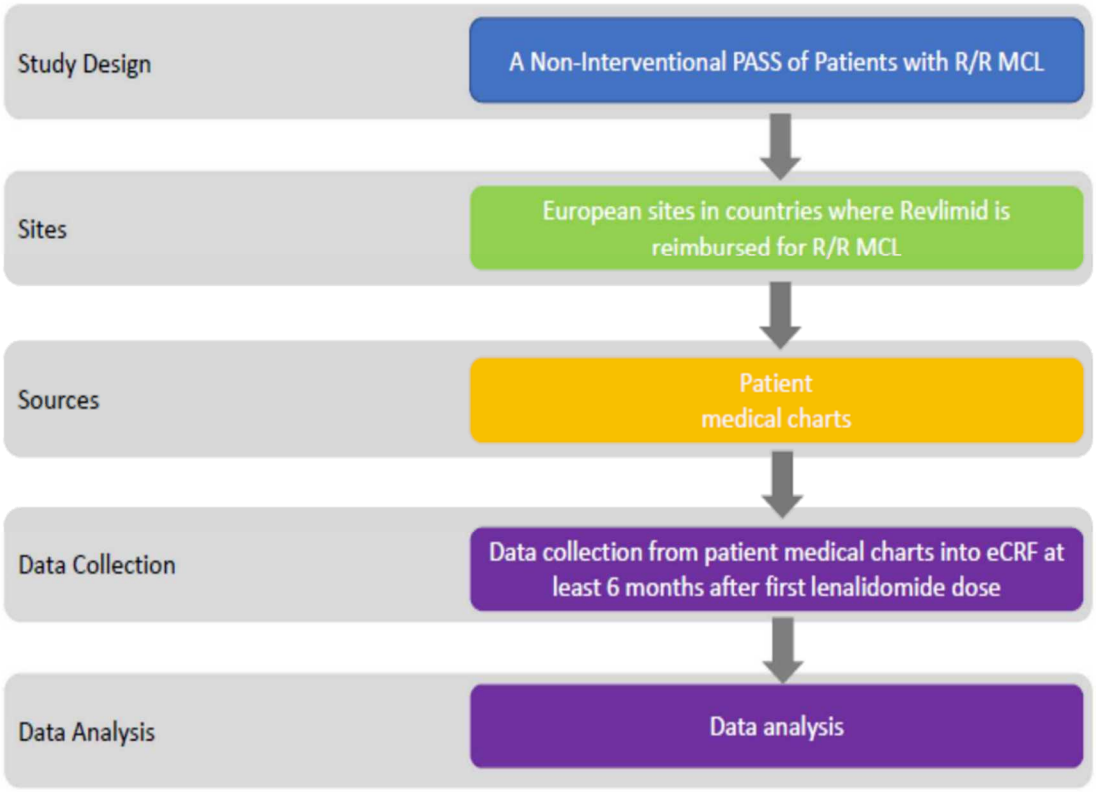
9 RESEARCH METHODS

9.1 STUDY DESIGN

This was a European multinational, retrospective, non-interventional study of patients with R/R MCL. Figure 9.1-1 provides a high-level schematic of the design of the study.

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Figure 9.1-1: Study Design



eCRF: electronic case report form; PASS: post-authorisation safety study; R/R MCL: relapsed or refractory mantle cell lymphoma

The study was performed in Europe. Potential sites were identified where R/R MCL patients were treated with lenalidomide and where lenalidomide was reimbursed for this indication. Identification of sites was done through partnerships such as, but not limited to that with the European Mantle Cell Lymphoma Registry. Other sources including knowledge of, or experience with sites could also be used for site identification purposes. Identified sites were assessed for feasibility and invited to participate in the study.

All data were collected retrospectively from identified patients following the first dose of lenalidomide treatment for up to 6 months including those patients who died within this data collection period.

9.2 SETTING

The study population consisted of a retrospective cohort of R/R MCL patients who had commenced treatment with lenalidomide after 08-Jul-2016 (date that marketing authorisation was granted).

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9.3 SUBJECTS

9.3.1 Inclusion Criteria

1) Received at least one dose of lenalidomide commencing after 08-Jul-2016 for the treatment of R/R MCL.
2) Informed consent of the patient or an authorised third person or authority, if required by law, given prior to data collection.
3) Patient was to be ≥18 years of age at the time of signing the informed consent form (ICF).

9.3.2 Exclusion Criteria

1) Patients were to be excluded if they were participating in an interventional clinical trial during the treatment period under observation in this PASS.

9.4 VARIABLES

Variables to be evaluated in this study included baseline demographic and clinical variables ("population dataset") (Table 9.4-1), treatment variables related to lenalidomide use and other relevant medications ("treatment dataset") (Table 9.4-2), and the outcome variables for safety ("outcomes dataset") (Table 9.4-3).

Table 9.4-1: Demographics and Clinical Variables

Variables	Data to be Collected
Demographics	
Age	Age (years)
Sex	Female/male
Clinical Variables	
Informed Consent	Date of consent
Date of Diagnosis	Date of initial MCL diagnosis, MIPI score at initial diagnosis, Bulky Disease at initial diagnosis
MCL	Date of initial MCL diagnosis; MIPI score at initial diagnosis; Bulky Disease at initial diagnosis; Prior stem cell transplantation (autologous/allogeneic); Date of last relapse/disease progression before lenalidomide therapy; Time from last dose of last therapy before lenalidomide therapy
Medical History	Prior history of TFR; Cardiovascular events (eg, arrhythmia and coronary artery disease); Cerebrovascular events (eg, TIA and stroke); Thromboembolic events (arterial and venous [eg, DVT, PE, and MI]); Peripheral/autonomic neuropathy; Pulmonary, hepatic, renal disease; History of other malignant diseases; Other relevant concomitant diseases or medical conditions

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Table 9.4-1: Demographics and Clinical Variables

Variables	Data to be Collected
Disease-related Characteristics	Tumour burden (high tumour burden is defined as at least one lesion of ≥ 5 cm diameter or at least 3 lesions of ≥3 cm diameter); Bulky disease (≥7 cm) at beginning of lenalidomide treatment; ECOG Performance Status
Relevant Concomitant Medications Related to TFR Treatment and/or Prophylaxis	Description of Concomitant Medication Indication of Concomitant Medication Start date of Concomitant Medication
Laboratory Tests	Haematology: haemoglobin, platelets, WBC, ANC, ALC Biochemistry: LDH, creatinine, creatinine clearance, blood glucose, bilirubin, albumin, ALT, AST, calcium, phosphorus, sodium, potassium, CRP
ECOG	ECOG status at baseline.

Abbreviations: ALC, absolute lymphocyte count; ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; CRP, C-reactive protein; DVT, deep vein thrombosis; ECOG, Eastern Cooperative Oncology Group; LDH, lactic dehydrogenase; MI, myocardial infarction; MCL, Mantle cell lymphoma; MIPI, Mantle Cell Lymphoma International Prognostic Index; PE, pulmonary embolism; TFR, tumour flare reaction; TIA, transient ischaemic attack; WBC, white blood cell.

Table 9.4-2: Lenalidomide Therapy and Other Treatment Variables

Variables	Data to be Collected
Previous Treatments	Number of previous lines of treatments, Description of previous treatments
Lenalidomide Treatments	Date of start and end of treatment [dd/mm/yyyy], lenalidomide dose and regimen, reason for lenalidomide discontinuation or any interruption of therapy with lenalidomide, dose adjustments (where applicable)

Table 9.4-3: Outcome Variables for Safety

Variables	Data to be Collected
TFR (Physician reported)	Adverse Event reported in eCRF/Medical file (onset date, stop date, severity, seriousness, clinical signs and symptoms, lab tests, treatment outcome [treatment discontinuation, dose interruption or dose reduction], relationship to lenalidomide)
TFR Symptoms and Signs	Painful lymph nodes, painful spleen enlargement, fever[a], rash[a], lymphocytosis[a]
Other AEs	Adverse events related to lenalidomide and not listed in current EU SmPC
Death	Date and cause of death, and method of documentation.

[a] Fever, rash, or lymphocytosis alone do not constitute TFR.
Abbreviations: AE, adverse event; eCRF, electronic case report form; EU, European Union; SmPC, Summary of Product Characteristics; TFR, tumour flare reaction

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A study flowchart provides additional details on the data that was collected before and during lenalidomide treatment (Table 9.4-4).

Table 9.4-4: Study Flow Chart Showing Collection of Data Before and During Course of Lenalidomide Treatment

	Pretreatment	During Treatment
Informed Consent[a]	NA	NA
Demographic Data	X	
Medical History	X	
MIPI Score	X	
Prior Stem Cell Transplantation	X	
ECOG PS	X	
Relevant Concomitant Medication	X	X
Tumour Burden Assessment	X[b]	
TFR Symptoms and Signs	X	X
Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC		X
Available Identified Laboratory Data[c]	X	X

[a] Patient informed consent, or agreement with a competent authority or another authorised third party (eg, next of kin), is to be obtained prior to data collection.

[b] Tumour burden assessment based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide.

[c] See laboratory tests in Table 9.4-3.

Abbreviations: CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EU, European Union; MIPI, Mantle Cell Lymphoma International Prognostic Index; SmPC, Summary of Product Characteristics; TFR, Tumour flare reaction.

9.5 DATA SOURCES AND MEASUREMENT

Data from individual patient medical charts were used as source data. The treating physician or an authorised delegate was to enter the data from these medical charts into the web-based electronic case report form (eCRF; secondary use of data). A common set of key variables (see Section 9.4) was collected. Data entry for each enrolled patient was only to start at least 6 months after the first dose of lenalidomide.

9.6 BIAS

All AEs (as documented in the medical charts) collected in the study that were related to lenalidomide but not listed in the current EU SmPC were summarised and frequencies calculated. Since the study was designed with TFR as the main outcome, it may not be sufficiently powered to provide a precise estimate for these adverse reactions. However, events captured through the review of medical records were an improvement on spontaneous reporting as these events may not have been captured through normal channels.

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Although a multivariable model was attempted to identify factors associated with TFR and early death, the sample size was not sufficiently powered and interpretation of results should be made with caution. There were also limitations to the Kaplan-Meier analysis as the retrospective nature of the study and the secondary use of the data did not allow for all the information needed with appropriate time precision and correspondence with the expected time to these events.

9.7 STUDY SIZE

Although the exact number of R/R MCL patients treated with lenalidomide in Europe was not known, internal data estimated the number of patients who receive second-line therapy in 5 countries of Europe (France, Germany, Italy, Spain and the United Kingdom) as 1,632 per year; and of those, 6% received lenalidomide alone or in combination with rituximab (Decision Resources Group internal data).

Additionally, an estimated 783 patients annually received ≥ third-line therapy, of which 11% were treated with lenalidomide alone or in combination with rituximab. The number of patients receiving lenalidomide for additional lines of therapy after third-line was expected to be very low. Based on these internal estimates, approximately 184 cases per year of R/R MCL patients potentially received second- or third-line lenalidomide treatment.

However, these estimates for treatment with lenalidomide are higher than published real-world data on treatment patterns for R/R MCL (2.3% to 2.7% usage of lenalidomide in second-line treatment).[1,2,3] Further limitations on the feasibility of recruiting patients included enrolling patients only in countries where lenalidomide was reimbursed, the introduction of new agents for R/R MCL, and a significant number of clinical trials for investigational agents in R/R MCL.

Therefore, based on the above, recruitment of a fixed number of 100 patients was considered feasible within the estimated study selection period.

Estimation of the Cumulative Incidence of TFR

The calculation of precision for the cumulative incidence of TFR was based upon the observed cumulative incidence of TFR (9.6%) in the CC-5013-MCL-002 study of 167 R/R MCL patients treated with lenalidomide with an exact two-sided 95% CI = (5.6%; 15.1%). From the CC-5013-MCL-002 study, there was a 20% chance that the cumulative incidence of TFR would exceed 12.0% (upper limit of the one-sided 80% CI). Under the assumption of a true TFR cumulative incidence rate of 9.6%, the precision on the estimate of the TFR cumulative incidence rate with 100 patients was 7.5% (upper limit of the exact two-sided 95% CI). Under the assumption of a true TFR cumulative incidence rate of 12% in the study population, the precision on the estimate of the TFR cumulative incidence rate with 100 patients was 8.0% (upper limit of the exact two-sided 95% CI).

Estimation of Early Death Rate

In Study CC-5013-MCL-002, 13.2% (22/167) of lenalidomide-treated patients died early (within 20 weeks from the first dose of lenalidomide). The exact two-sided 95% CI was (8.4%; 19.3%), and there was only a 20% chance that the early death rate would exceed 15.9% (upper limit of the one-sided 80% CI). With 100 patients, the study allowed a calculation of the early death rate with

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a precision of +8.2% for the upper limit of the exact two-sided 95% CI for an observed rate of 13.2%, and +8.7% for an observed rate of 15.9%.

9.8 DATA TRANSFORMATION

Data for the MCL PASS were collected once patient records were complete, ie, if 6 months had elapsed after a patient received the first lenalidomide dose.

The data were collected using an eCRF. For each patient, data were collected in compliance with the applicable local legislation.

The data collected via an eCRF were electronically verified through use of programmed edit checks. Discrepancies in the data were brought to the attention of the team, and investigational site personnel, if necessary. Resolution of these issues was reflected in the database. An audit trail within the system tracked all changes made to the data.

Study Monitoring and Source Data Verification

The sponsor was to ensure that appropriate quality review procedures were performed during and after data collection. Accuracy was checked through programmatic edit checks according to the standard quality control procedures at the institutions conducting the data collection. The contract research organisation (CRO) issued queries to the site for resolution. Any necessary corrections were then applied to the data in the eCRF. If necessary, source data verification (ie, a direct comparison of the entries made in the eCRF against the patient's notes) could be conducted in a selected subgroup of sites.

9.9 STATISTICAL METHODS

The statistical analysis is detailed in the statistical analysis plan (SAP, see Appendix 1.5).

9.9.1 Main Summary Measures

Summary statistics consisted of the number and percentage of in each category for discrete variables, and the sample size, minimum, maximum, median, mean and standard deviation for continuous variables.

Unless specified otherwise, confidence intervals were presented as 2-sided at the 95% level.

9.9.2 Main Statistical Methods

9.9.2.1 General Methods

- The day of the first dose of lenalidomide after the diagnosis of R/R MCL was defined as Day 1.
- Baseline date was defined as the date of first dose of lenalidomide (Day 1).
- Baseline value was defined as the last value on or within a specific time window before the baseline date (see Section 5.2.3 in the SAP [Appendix 1.5]). If multiple values were present for the same date, the average of these values was used as the baseline, except otherwise specified.
- Patient's age in the inclusion criteria was the age at ICF signing, or, if not available, the age at the first dose of lenalidomide. The baseline age was that at the baseline date.

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- If there were multiple post-treatment laboratory measures of the same type from one patient, the mean was used in the analysis.

9.9.2.2 Primary Objective

The analysis for the primary objective was performed primarily on the Per Protocol Analysis Set (PPAS) and on the Safety Analysis Set (SAS) for sensitivity analysis, as the two sets were different. The analyses were stratified according to the tumour burden at baseline (low vs. high tumour burden at baseline).

The primary objective of the study was estimated by the cumulative incidence (and exact two-sided 95% CI) of TFR that occurred within the date of first dose of lenalidomide and up to 6 months past the date of first dose of lenalidomide. The cumulative incidence was calculated as the ratio:

$$\frac{\#\ of\ Patients\ with\ at\ least\ 1\ TFR\ event}{\#\ of\ Patients\ in\ the\ Analysis\ Set}$$

In addition, the Incidence Rate of TFR per 100 person-years (PY; with 95% CIs) was calculated as the ratio:

$$\frac{\#\ of\ Patients\ with\ at\ least\ 1\ TFR\ event}{Total\ Person\ Years} \cdot 100$$

The total person-years was defined as the total time from the first lenalidomide dose date to the first date of TFR for patients reporting TFR. For patients reporting no TFR event during the 6-month period following the first lenalidomide dose the following censoring rules apply:

- Any patient for whom information may exist in the source database after the 6-month period following the first lenalidomide dose was censored at 6 months.
- Any patient for whom no information exists in the source database at the end of the 6-month study period was censored at the date of the last information available in the 6-month period.

The 95% CI for the Incidence Rate (IR) per 100 PY was calculated using the delta method:

$$IR * \exp\{\pm 1.96\ /\ square\ root\ of\ n\}$$

where n is the number of events observed.

Where sufficient data was available, the number of TFR event per patient was tabulated.

Time to TFR was also planned to be analysed using the Kaplan-Meier (KM) method. Since data were collected retrospectively, the number of time points each patient may have was unknown a priori. Given that the precision of the KM method varied with the number of time points available for analysis and that TFR was likely to occur early in treatment with lenalidomide (time to TFR is less than 5 days for almost 25% of patients experiencing TFR and the interquartile range for time to TFR in Study MCL-002 is [0.7, 2.4] weeks[4]), there was likely an impact on the precision of the estimate using this method.

Consequently, KM analyses were not performed as primary but planned as complementary analyses. KM curves were planned to be provided for time to first TFR event. For KM analyses, the same censoring rules were planned to be applied to compute the Incidence Rates. Death related

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to a TFR event was planned to be considered as an event. Death unrelated to TFR were planned to be considered as a censoring event for the Kaplan Meier analysis.

9.9.2.3 Secondary Objectives

The analysis for the secondary objective was performed primarily on the PPAS and on the SAS for sensitivity analysis, as the two sets were different. All analyses were stratified according to the tumour burden at baseline (low vs. high tumour burden at baseline).

The secondary endpoint was estimated by the cumulative incidence of early death, defined as any death occurring within 20 weeks from the first dose of lenalidomide. The exact two-sided 95% CIs were calculated. The cumulative incidence of early death was calculated as the ratio:

$$\frac{\#\ of\ Patients\ with\ Early\ Death}{\#\ of\ Patients\ in\ the\ Analysis\ Set}$$

Time to early death was analysed using the KM method. KM curves were provided for time to early death. For patients with no death reported within 20 weeks after the first dose of lenalidomide, the following censoring rules were used:

- Any patient for whom information existed in the source database after the 20-week period following the first lenalidomide dose was censored at 20 weeks.
- Any patient for whom no information existed in the source database at the end of the 20-week period was censored at the date of the last information available in the 20-week period.

9.9.2.4 Exploratory Analyses

9.9.2.4.1 Exploration of Risk Factors Associated with TFR

If there were ≥ 5 TFR events, exploration of factors associated with TFR was conducted in multivariable analyses procedure using Cox models to fit time-to-event data. Factors for consideration included:

- Age, Sex
- Country, site
- History of TFR (yes or no) at baseline
- Tumour burden at baseline (last available information prior to lenalidomide 1st dose).
- Bulky Disease at baseline
- ECOG PS at baseline

Other risk factors for TFR could be added.

The procedure was performed by first screening all baseline risk factors in a univariable setting. Those risk factors that had a statistically significant association with the outcome at 0.20 level ($p < 0.20$) were included in the multiple regression model. The final model was determined on the complete dataset using a backward elimination variable-selection procedure with $p > 0.10$ as the significance criterion for elimination.

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The estimated Hazard Ratios with 95% confidence intervals and p-values were presented for the univariable regressions and for the risk factors retained in the final multivariable model.

9.9.2.4.2 Exploration of Risk Factors Associated with Early Death

If there were ≥ 5 TFR events, exploration of factors associated with early death was conducted in multivariable procedure using Cox models to fit time-to-event data. Factors to be included in the models were:

- Age, Sex
- Country, site
- History of TFR (yes or no) at baseline
- Tumour burden at baseline (last available information prior to lenalidomide 1st dose).
- Bulky Disease at baseline
- ECOG PS at baseline

Other risk factors for early death could be added.

The analysis was performed by first screening all baseline risk factors in a univariable setting. Those risk factors that had a statistically significant association with the outcome at 0.20 level ($p < 0.20$) were included in the multiple regression model. The final model was determined on the complete dataset using a backward elimination variable-selection procedure with $p > 0.10$ as the significance criterion for elimination.

The estimated Hazard Ratios with 95% confidence intervals and p-values were presented for the univariable regressions and for the risk factors retained in the final multivariable model.

9.9.2.5 Analysis Populations

Safety Analysis Set

The SAS included all patients present in the clinical database who received at least one dose of Lenalidomide but not necessarily met all the inclusion/exclusion criteria.

Per Protocol Analysis Set

The PPAS included patients enrolled in the study who met all the inclusion/exclusion criteria.

Results were presented for the PPAS. As the SAS contained additional patients, analyses for the primary and secondary endpoints were repeated on the SAS as sensitivity analysis.

9.9.2.6 Patient Disposition

The total number of patients enrolled in the study was summarised. A summary of patient disposition was presented for the SAS.

9.9.2.7 Protocol Deviations

Protocol deviations were reported for the SAS (See Section 10.1.2).

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9.9.2.8 Descriptive Analyses

The demographics, disease related characteristics and baseline characteristics were summarised for the PPAS.

9.9.2.8.1 Demographics

Patients demographics (age and sex) were listed and tabulated with appropriate summary statistics.

9.9.2.8.2 MCL Diagnosis and Disease-related characteristics

The time from initial diagnosis to first dose of lenalidomide was calculated as (first lenalidomide dose date - date of diagnosis +1) / 30.4375.

The MIPI score, Bulky disease status, B-symptoms presence, Ann Arbor stage and Cyclin D1 detection at initial diagnosis were tabulated.

9.9.2.8.3 Baseline characteristics

The time from relapse / disease progression to first dose of lenalidomide and the time from last dose of last therapy to first dose of lenalidomide were presented.

The MIPI score, the ECOG PS, Bulky disease status, B-symptoms presence, Ann Arbor stage, Cyclin D1 detection, history of TFR and high tumour burden at baseline were tabulated.

The proportion of patients with high tumour burden at baseline was estimated with its two-sided 95% CI. In this study, high tumour burden was defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.

9.9.2.8.4 Medical History

Medical and surgical history was coded using the Medical Dictionary for Drug Regulatory Activities (MedDRA) version 26.0 or later. System organ class and preferred term were summarised by frequency and percentage.

9.9.2.8.5 Prior Therapies and Concomitant Medications

All medications including prior therapies and concomitant medications were coded using the World Health Organisation (WHO) Drug Global dictionary terms in the 2023 or the latest version.

Prior Therapies (Including Surgery)

Frequency tabulations of the number of patients with at least one prior therapy, the frequency of the number of prior therapies and type of previous therapies (chemotherapy, immunotherapy, stem cell transplant [separating autologous from allogeneic if possible], radiation, anthracycline/mitoxantrone or cyclophosphamide or rituximab or bortezomib-containing regimens, etc.) were provided for the PPAS.

Concomitant Medications

Concomitant medications were defined as medications that were either initiated before the first lenalidomide dose date and continued during the lenalidomide treatment or initiated on/after the first lenalidomide dose date and strictly before the date of treatment discontinuation.

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A summary showing the number and percentage of patients who took concomitant medications was presented by WHO therapeutic drug class and generic drug name for the PPAS.

9.9.2.8.6 Clinical Laboratory Evaluations

Clinical laboratory values at baseline were presented by summary statistics (n, mean, standard deviation, median, minimum, and maximum) for the PPAS.

9.9.2.8.7 Lenalidomide Treatment and Extent of Exposure

Lenalidomide treatment duration was provided based on the PPAS. Descriptive statistics were provided for treatment duration.

The lenalidomide duration (weeks) was defined as:

[(lenalidomide stop date) – (first lenalidomide start date) + 1]/7.

For patients who were still on lenalidomide at the time of study closure or analysis time, the clinical cutoff date was used as the lenalidomide end date.

Cumulative dose, defined as the sum of all doses taken across the treatment period in mg was tabulated.

9.9.2.9 Efficacy Analysis

No efficacy analysis was performed.

The best response achieved was tabulated by frequency for the PPAS.

9.9.2.10 Safety Analysis

9.9.2.10.1 Primary Safety Analysis

The frequency of TFR was reported in summary tables for the PPAS.

TFR was characterised by clinical assessments and laboratory tests, and tabulated by frequency, severity, seriousness, tumour burden, time to onset, treatment outcome (treatment discontinuation, dose interruption or dose reduction), time to resolution, and relationship to lenalidomide.

Death was summarised as the frequency of patients who experienced death, and as primary cause of death. Early death was summarised as the frequency of patients who experienced early death (defined as any death occurring within 20 weeks of the initial administration of lenalidomide), and as primary cause of early death.

9.9.2.10.2 Analysis of Other Adverse Events

Only TEAEs related to lenalidomide that were not listed in the current Revlimid EU SmPC (Version 58.0 approved on 09-Feb-2023) were reported in this study.

All TEAEs were coded using MedDRA version 26.0 or later. Treatment-related TEAE was defined as TEAE, which was considered to be related to the lenalidomide treatment by the investigator.

If a patient experienced the same TEAE more than once with different toxicity grades, the event with the highest grade was tabulated in “by grade” tables.

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If a patient experience multiple TEAEs under the same preferred term PT (System Organ Class [SOC]), then the patient was counted only once for that PT (SOC).

The incidence of TEAEs related to lenalidomide was summarised by MedDRA SOC and PT. The intensity of TEAEs was graded 1 to 5 according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.

As the SAS contained additional patients, analyses of TEAEs were to be repeated on the SAS as sensitivity analysis.

9.9.3 Missing Values

No imputations were performed, except for partially missing dates (see Section 3.4.4.2 of the SAP).

9.9.4 Sensitivity Analyses

Results were presented for the PPAS. As the SAS contained additional patients, analyses for the primary and secondary endpoints were repeated on the SAS as sensitivity analysis.

9.9.5 Amendments to the Statistical Analysis Plan

None.

9.10 QUALITY CONTROL

All data collected for the study were to be recorded accurately. Security of the data was maintained at all times in line with applicable local law and procedures.

Access was limited to authorised individuals. Controls, such as document encryption, were used to ensure the authenticity, integrity, and confidentiality of electronic records when transmitted over open systems (eg, the internet). Adequate back up of the data was maintained throughout the course of the study.

The following activities aimed to ensure data quality by checking the accuracy of the data collected from medical charts, checking the completeness and validity of data in the electronic data capture (EDC) through:

- Monitoring:
  - Performing source data verification (samples rather than 100%) to ensure EDC data match source data
- Data Management:
  - Using edit checks mainly within the EDC system for more efficient data cleaning and for identification of critical missing data, required data fields, illogical, and inconsistent data

10 RESULTS

10.1 PARTICIPANTS

10.1.1 Patient Disposition

Data were collected from 02-Oct-2018 (first patient enrolled) through 10-Jan-2024 (last patient last visit). The database lock date was 20-Feb-2024.

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In total, 105 patients were screened. Among these, 101 (96.2%) were eligible to comprise the PPAS; 4 patients (3.8%) did not meet the eligibility criteria (3 patients did not receive lenalidomide commencing after 08-Jul-2016 for the treatment of R/R MCL and 1 patient was participating in an interventional clinical trial during the treatment period under observation in this PASS) (Appendix 1.6, Table 14.1.1).

Study completion and study discontinuation for patients in the PPAS and patients in the SAS are presented in Table 10.1.1-1.

In the PPAS, 71 patients (70.3%) completed the study and 30 (29.7%) discontinued the study. The reasons for study discontinuation consisted of death (26 patients [25.7%]) and lost to follow-up (4 patients [4.0%]).

Of the 105 screened patients, 103 patients (98.1%) received at least one dose of treatment and were included in the SAS (Appendix 1.6, Table 14.1.2). Analyses pertaining to the primary and secondary endpoints were repeated on the SAS as sensitivity analysis (see Section 10.4.1 and Section 10.4.2). As the SAS and PPAS cohorts were nearly identical (the SAS included 2 additional patients), the results in the PPAS and the results of the sensitivity analyses in the SAS were very similar.

In the SAS, 71 patients (68.9%) completed the study, 2 (1.9%) were screen failures, and 30 (29.1%) discontinued the study. The reasons for study discontinuation were death (26 patients [25.2%]) and loss to follow-up (4 patients [3.9%]).

Patient disposition is provided by patient in Appendix 1.7, Listing 16.2.1.1. Information on study discontinuation (including screen failure) is provided by patient in Appendix 1.7, Listing 16.2.1.2. Information on study analysis population is provided by patient in Appendix 1.7, Listing 16.2.1.3.

Table 10.1.1-1: Patient Disposition – Per Protocol Analysis Set and Safety Analysis Set

Parameter	PPAS (N=101) n (%)[a]	SAS (N=103) n (%)[b]
Patients who Completed the Study	71 (70.3)	71 (68.9)
Screen Failures	0 (0.0)	2 (1.9)
Patients who Discontinued the Study	30 (29.7)	30 (29.1)
Reason for Study Discontinuation		
Death	26 (25.7)	26 (25.2)
Lost to Follow-up	4 (4.0)	4 (3.9)

[a] Percentages are calculated using the PPAS.

[b] Percentages are calculated using the SAS.

Abbreviations: PPAS, Per Protocol Analysis Set; SAS, Safety Analysis Set.

Source: Table 14.1.3.1, Table 14.1.3.2

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10.1.2 Protocol Deviations

Protocol deviations that occurred during the study are summarised in Table 10.1.2-1.

Protocol deviations were reported in 13 patients (12.9%). Protocol deviations consisted of ICF issues (12 patients) and other issues (3 patients).

None of these protocol deviations affected the overall quality or interpretation of the study data.

Protocol deviations in enrolled patients is provided by patient in Appendix 1.7, Listing 16.2.2.

Table 10.1.2-1: Protocol Deviations - Per Protocol Analysis Set

Parameter	Total (N=101)
Number of Patients with at Least One Protocol Deviation	13 (12.9)
ICF ISSUES	12 (11.9)
OTHER	3 (3.0)

Patients may have more than one protocol deviation.
Source: Table 14.1.7

10.2 DESCRIPTIVE DATA

10.2.1 Demographics

Demographics are summarised for the PPAS in Table 10.2.1-1.

In the PPAS, the median age was 74.0 years (min: 44, max: 91), 85.1% of patients were ≥65 years. The proportion of male patients was 79.2%.

Demographics in the PPAS are provided by patient in Appendix 1.7, Listing 16.2.4.2.1.

Table 10.2.1-1: Demographics – Per Protocol Analysis Set

Parameter	Total (N=101)
Sex, n (%)	
n (%)	101 (100.0)
Male	80 (79.2)
Female	21 (20.8)
Missing, n (%)	0 (0.0)
Age (years)	
n (missing)	101 (0)
Mean	73.4
SD	8.83
Median	74.0

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Table 10.2.1-1: Demographics – Per Protocol Analysis Set

Parameter	Total (N=101)
Q1, Q3	68.0, 80.0
Min, Max	44, 91
Age Categories (years), n (%)	
n (%)	101 (100.0)
<65	15 (14.9)
>=65	86 (85.1)
Missing, n (%)	0 (0.0)
n (%)	101 (100.0)
<75	52 (51.5)
>=75	49 (48.5)
Missing, n (%)	0 (0.0)

Max: Maximum; Min: Minimum; Q1: First quartile; Q3: Third quartile; SD: Standard deviation.
Percentages are calculated using the number of patients with available (non-missing) data.
Source: Table 14.1.4

10.2.2 Baseline Characteristics

Disease-related characteristics at the time of MCL diagnosis are summarised for the PPAS in Table 10.2.2-1.

In the PPAS, the median time from initial MCL diagnosis to start of lenalidomide was 51.0 months (min: 2, max: 207). The MIPI score at diagnosis was low risk in 8.9%, intermediate risk in 17.8%, and high risk in 31.7% of patients (unknown in 41.6% of patients).

At diagnosis, 10.9% of patients had bulky disease. Presence of B-symptoms was reported in 25.7% of patients. t(14;18) translocation was reported in 12.4% of patients. Ann Arbor stage was stage I in 2.0%, stage II in 0.0%, stage III in 6.9%, and stage IV in 79.2% (unknown in 11.9% of patients). Positive cyclin D1 was reported in 64.4% of patients (Appendix 1.6, Table 14.1.5).

MCL diagnosis and disease-related characteristics in the PPAS are provided by patient in Appendix 1.7, Listing 16.2.4.1.

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Table 10.2.2-1: Disease-related Characteristics at the Time of MCL Diagnosis – Per Protocol Analysis Set

Parameter	Total (N=101)
Time from Initial MCL Diagnosis to Start of Lenalidomide (months)[a]	
n (missing)	101 (0)
Mean	66.1
SD	46.03
Median	51.0
Q1, Q3	35.5, 87.4
Min, Max	2, 207
MIPI Score at Diagnosis, n (%)	
n (%)	101 (100.0)
Low Risk	9 (8.9)
Intermediate Risk	18 (17.8)
High Risk	32 (31.7)
Unknown[b]	42 (41.6)
Missing, n (%)	0 (0.0)
Bulky Disease at Diagnosis, n (%)	
n (%)	101 (100.0)
Yes	11 (10.9)
No	65 (64.4)
Unknown[b]	25 (24.8)
Missing, n (%)	0 (0.0)

[a] Time from initial MCL diagnosis to start of lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of initial MCL diagnosis + 1) /30.4375].

[b] Unknown = the assessment was done, but the result is not known.

Abbreviations: Max, Maximum; MCL, Mantle Cell Lymphoma; Min, Minimum; MIPI, Mantle Cell Lymphoma International Prognostic Index; Q1, First quartile; Q3, Third quartile; SD, Standard deviation.

Percentages are calculated using the number of patients with available (non-missing) data.

Source: Table 14.1.5

Baseline characteristics are summarised for the PPAS in Table 10.2.2-2.

At baseline, relapse or refractory MCL was reported in 100% of patients. The median time from relapse/progression to start of lenalidomide was 0.85 months (min: 0.0, max: 114.3). The median time from last dose of last therapy to start of lenalidomide was 2.10 months (min: 0.0, max: 113.4). The proportion of patients in the low, intermediate, and high risk MIPI score categories at baseline was 7.9%, 7.9%, and 20.8%, respectively (unknown in 63.4% of patients). At baseline, 12.9% of patients had bulky disease. At baseline, 85.5% of patients had an ECOG performance status of 0

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or 1. History of TFR was reported in 5.0% of patients. At baseline, the proportion of patients with high tumour burden was 14.9% (95% CI: 8.6%, 23.3%). Tumour burden was unreported at baseline (missing or unknown) for 38 patients (37.6%). Presence of B-symptoms was reported in 7.9% of patients. Ann Arbor stage at baseline was stage I in 1.0%, stage II in 4.0%, stage III in 7.9%, and stage IV in 44.6% (unknown in 42.6% of patients).

Baseline characteristics in the PPAS are provided by patient in Appendix 1.7, Listing 16.2.4.2.2.

Table 10.2.2-2: Baseline Characteristics – Per Protocol Analysis Set

Parameter	Total (N=101)
Relapse or Refractory MCL, n (%)	
n (%)	101 (100.0)
Yes	101 (100.0)
No	0 (0.0)
Missing, n (%)	0 (0.0)
Time from Relapse/Progression to Start of Lenalidomide (months)[a]	
n (missing)	95 (6)
Mean	4.13
SD	13.395
Median	0.85
Q1, Q3	0.30, 2.23
Min, Max	0.0, 114.3
Time from Last Dose of Last Therapy to Start of Lenalidomide (months)[b]	
n (missing)	92 (9)
Mean	11.73
SD	21.533
Median	2.10
Q1, Q3	0.64, 11.07
Min, Max	0.0, 113.4
MIPI Score at Baseline, n (%)	
n (%)	101 (100.0)
Low Risk	8 (7.9)
Intermediate Risk	8 (7.9)
High Risk	21 (20.8)
Unknown	64 (63.4)
Missing, n (%)	0 (0.0)

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Table 10.2.2-2: Baseline Characteristics – Per Protocol Analysis Set

Parameter	Total (N=101)
Bulky Disease at Baseline, n (%)	
n (%)	101 (100.0)
Yes	13 (12.9)
No	61 (60.4)
Unknown	27 (26.7)
Missing, n (%)	0 (0.0)
ECOG Performance Status at Baseline, n (%)	
n (%)	62 (61.4)
0	30 (48.4)
1	23 (37.1)
2	7 (11.3)
3	2 (3.2)
4	0 (0.0)
5	0 (0.0)
Unknown	0 (0.0)
Missing, n (%)	39 (38.6)
History of Tumour Flare Reaction, n (%)	
n (%)	101 (100.0)
Yes	5 (5.0)
No	96 (95.0)
Unknown	0 (0.0)
Missing, n (%)	0 (0.0)
High Tumour Burden at Baseline, n (%)[c]	
n (%)	101 (100.0)
Yes	15 (14.9)
No	48 (47.5)
Unknown	38 (37.6)
Missing, n (%)	0 (0.0)
Proportion of Patients with High Tumour Burden at Baseline, n (%)	15 (14.9)
[95% CI]	[8.6, 23.3]

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Table 10.2.2-2: Baseline Characteristics – Per Protocol Analysis Set

Parameter	Total (N=101)
B-symptoms Presence at Baseline, n (%)	
n (%)	101 (100.0)
Yes	8 (7.9)
No	62 (61.4)
Unknown	31 (30.7)
Missing, n (%)	0 (0.0)
Ann Arbor Stage at Baseline, n (%)	
n (%)	101 (100.0)
Stage I	1 (1.0)
Stage II	4 (4.0)
Stage III	8 (7.9)
Stage IV	45 (44.6)
Unknown	43 (42.6)
Missing, n (%)	0 (0.0)

[a] Time Relapse/Progression to Start of Lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of Relapse/Progression + 1)/30.4375].

[b] Time from Last Dose of Last Therapy to Start of Lenalidomide is calculated as [(Date of last dose of last therapy - Date of 1st dose of lenalidomide + 1)/30.4375].

[c] High tumour burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.

Abbreviations: ECOG, Eastern Cooperative Oncology Group; Max, Maximum; MCL, Mantle Cell Lymphoma; Min, Minimum; MIPI, Mantle Cell Lymphoma International Prognostic Index; Q1, First quartile; Q3, Third quartile; SD, Standard deviation.

Percentages are calculated using the number of patients with available (non-missing) data.

For pre-baseline measures to be considered as of baseline, the measure must fall in a specific time window prior to the Date of 1st dose of lenalidomide. Time windows for all variables at baseline are specified in the statistical analysis plan.

Source: Table 14.1.6

10.2.3 Medical History

Medical history is summarised for the PPAS in Table 10.2.3-1 and Table 10.2.3-2.

Prior medical history was reported in 56.4% of patients. The most frequent prior conditions reported were infections and infestations (16.8%), neoplasms benign, malignant, and unspecified (including cysts and polyps) (16.8%), cardiac disorders (12.9%), and gastrointestinal disorders (11.9%).

Concomitant medical history was reported in 76.2% of patients. The most frequent concomitant conditions reported were vascular disorders (29.7%), cardiac disorders (23.8%), metabolism and

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nutrition disorders (21.8%), respiratory, thoracic and mediastinal disorders (16.8%), and musculoskeletal and connective tissue disorders (13.9%).

Medical history is provided by patient in Appendix 1.7, Listing 16.2.4.4.

Table 10.2.3-1: Medical History: Prior Condition (PT Reported in ≥2% of Patients) – Per Protocol Analysis Set

System Organ Class Preferred Term[a]	Total (N=101) n (%)
Patients With at Least One Medical History Condition	57 (56.4)
Infections and Infestations	17 (16.8)
Pneumonia	3 (3.0)
Neoplasms Benign, Malignant and Unspecified (incl. cysts and polyps)	17 (16.8)
Basal Cell Carcinoma	2 (2.0)
Breast Cancer	2 (2.0)
Renal Cell Carcinoma	2 (2.0)
Uterine Leiomyoma	2 (2.0)
Cardiac Disorders	13 (12.9)
Atrial Fibrillation	4 (4.0)
Acute Myocardial Infarction	3 (3.0)
Atrioventricular Block	2 (2.0)
Gastrointestinal Disorders	12 (11.9)
Diverticulum	4 (4.0)
Inguinal Hernia	3 (3.0)
Musculoskeletal and Connective Tissue Disorders	7 (6.9)
Intervertebral Disc Protrusion	3 (3.0)
Renal and Urinary Disorders	7 (6.9)
Nephrolithiasis	2 (2.0)
Renal Colic	2 (2.0)
Respiratory, Thoracic and Mediastinal Disorders	7 (6.9)
Pleural Effusion	3 (3.0)
Pulmonary Embolism	2 (2.0)
Vascular Disorders	7 (6.9)
Deep Vein Thrombosis	3 (3.0)
Hypertension	2 (2.0)
Nervous System Disorders	6 (5.9)
Transient Ischaemic Attack	2 (2.0)

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Table 10.2.3-1: Medical History: Prior Condition (PT Reported in ≥2% of Patients) – Per Protocol Analysis Set

System Organ Class Preferred Term[a]	Total (N=101) n (%)
Hepatobiliary Disorders	3 (3.0)
Cholelithiasis	2 (2.0)
Metabolism and Nutrition Disorders	3 (3.0)
Dyslipidaemia	2 (2.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary are classified as 'Not Coded'.
Source: Table 14.1.8.1

Table 10.2.3-2: Medical History: Concomitant Condition (PT Reported in ≥2% of Patients) – Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Patients With at Least One Medical History Condition	77 (76.2)
Vascular Disorders	30 (29.7)
Hypertension	27 (26.7)
Cardiac Disorders	24 (23.8)
Atrial Fibrillation	12 (11.9)
Coronary Artery Disease	5 (5.0)
Ischaemic Cardiomyopathy	2 (2.0)
Mitral Valve Incompetence	2 (2.0)
Myocardial Ischaemia	2 (2.0)
Metabolism and Nutrition Disorders	22 (21.8)
Dyslipidaemia	7 (6.9)
Type 2 Diabetes Mellitus	7 (6.9)
Diabetes Mellitus	5 (5.0)
Hypercholesterolaemia	4 (4.0)
Hyperlipidaemia	2 (2.0)
Hyperuricaemia	2 (2.0)
Respiratory, Thoracic and Mediastinal Disorders	17 (16.8)
Chronic Obstructive Pulmonary Disease	7 (6.9)

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Table 10.2.3-2: Medical History: Concomitant Condition (PT Reported in ≥2% of Patients) – Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Obstructive Sleep Apnoea Syndrome	2 (2.0)
Sleep Apnoea Syndrome	2 (2.0)
Musculoskeletal and Connective Tissue Disorders	14 (13.9)
Osteoarthritis	7 (6.9)
Osteoporosis	3 (3.0)
Rheumatoid Arthritis	2 (2.0)
Spinal Stenosis	2 (2.0)
Blood and Lymphatic System Disorders	10 (9.9)
Anaemia	6 (5.9)
Neutropenia	2 (2.0)
Thrombocytopenia	2 (2.0)
Renal and Urinary Disorders	9 (8.9)
Chronic Kidney Disease	5 (5.0)
Reproductive System and Breast Disorders	8 (7.9)
Benign Prostatic Hyperplasia	7 (6.9)
Eye Disorders	6 (5.9)
Glaucoma	4 (4.0)
Endocrine Disorders	5 (5.0)
Hyperthyroidism	2 (2.0)
Neoplasms Benign, Malignant and Unspecified (incl. cysts and polyps)	5 (5.0)
Prostate Cancer	2 (2.0)
Infections and Infestations	4 (4.0)
Hepatitis B	2 (2.0)
Immune System Disorders	3 (3.0)
Hypogammaglobulinaemia	2 (2.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary are classified as 'Not Coded'.
Source: Table 14.1.8.2

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10.2.4 Prior and Concomitant Medications

10.2.4.1 Prior Systemic Anti-Cancer Therapies

Prior anti-cancer therapies are summarised for the PPAS in Table 10.2.4.1-1. Prior anti-cancer therapies are provided in Appendix 1.6, Table 14.1.9.2.

The percentage of patients with at least one prior systemic therapy was 97.0%. Overall, 55.4% of patients had 1 previous line of therapy, 28.7% had 2 previous lines of therapy, and 14.8% had ≥3 previous lines of therapy. Prior stem cell transplant was reported in 24.8% of patients (autologous in 24.8% and allogenic in 2.0%).

The best response achieved prior to lenalidomide was complete response (73.5% of patients), partial response (16.3%), and stable disease (5.1%).

The most common prior systemic anti-cancer therapies were rituximab (93.1%), bendamustine (65.3%), cyclophosphamide (56.4%), cytarabine (46.5%), doxorubicin (46.5%), ibrutinib (45.5%), and vincristine (36.6%). Additionally, 37.6% of patients were treated with dexamethasone and 34.7% with prednisone.

Prior anti-cancer therapies are provided by patient in Appendix 1.7, Listing 16.2.4.5.1.

Table 10.2.4.1-1: Prior Anti-Cancer Therapies Summary – Per Protocol Analysis Set

Parameter	Total (N=101) n (%)
Patients with at Least One Prior Systemic Therapy[a]	98 (97.0)
Number of Previous Lines of Therapy[b]	
n (%)	101 (100.0)
0	1 (1.0)
1	56 (55.4)
2	29 (28.7)
3	7 (6.9)
4+	8 (7.9)
Unknown	0 (0.0)
Missing, n (%)	0 (0.0)
Prior Stem Cell Transplant	
n (%)	101 (100.0)
Yes	25 (24.8)
Autologous	25 (24.8)
Allogeneic	2 (2.0)
Unknown	0 (0.0)

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Table 10.2.4.1-1: Prior Anti-Cancer Therapies Summary – Per Protocol Analysis Set

Parameter	Total (N=101) n (%)
No	76 (75.2)
Unknown	0 (0.0)
Missing, n (%)	0 (0.0)
Best Response Achieved Prior to Lenalidomide[c]	
n (%)	98 (97.0)
Complete Response	72 (73.5)
Partial Response	16 (16.3)
Stable Disease	5 (5.1)
Progressive Disease	0 (0.0)
Not Evaluable	0 (0.0)
Unknown	5 (5.1)
Missing, n (%)	3 (3.0)

[a] Prior Anti-Cancer Therapies as any treatment taken and discontinued prior to the 1st dose of lenalidomide.
[b] Number of lines of therapy which started prior to the 1st dose of lenalidomide.
[c] Best response achieved among prior anti-cancer therapies, that is, any therapy which discontinued prior to the 1st dose of lenalidomide.
Percentages are calculated using the number of patients with available (non-missing) data.
Source: Table 14.1.9.1

10.2.4.2 Concomitant Medications

Concomitant medications are summarised in Table 10.2.4.2-1.

Concomitant medications were reported in 66.3% of patients. The most common ATC classes were blood and blood forming organs (48.5%), antiinfectives for systemic use (39.6%), alimentary tract and metabolism (37.6%), and cardiovascular system (29.7%).

Concomitant medications other than for MCL are provided by patient in Appendix 1.7, Listing 16.2.4.5.2.

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Table 10.2.4.2-1: Concomitant Medications (Preferred Name Reported in ≥4% of Patients) - Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name[a]	Total (N=101)
Patients with at Least One Concomitant Medication	67 (66.3)
Blood and Blood Forming Organs	49 (48.5)
Acetylsalicylic Acid	16 (15.8)
Enoxaparin Sodium	5 (5.0)
Acetylsalicylate Lysine	4 (4.0)
Apixaban	4 (4.0)
Antiinfectives for Systemic Use	40 (39.6)
Sulfamethoxazole;trimethoprim	20 (19.8)
Aciclovir	12 (11.9)
Valaciclovir Hydrochloride	6 (5.9)
Lamivudine	5 (5.0)
Levofloxacin	4 (4.0)
Valaciclovir	4 (4.0)
Alimentary Tract and Metabolism	38 (37.6)
Omeprazole	14 (13.9)
Colecalciferol	7 (6.9)
Lansoprazole	6 (5.9)
Pantoprazole Sodium Sesquihydrate	6 (5.9)
Metformin	4 (4.0)
Cardiovascular System	30 (29.7)
Furosemide	8 (7.9)
Bisoprolol Fumarate	6 (5.9)
Ramipril	6 (5.9)
Amlodipine	4 (4.0)
Simvastatin	4 (4.0)
Musculo-skeletal System	20 (19.8)
Allopurinol	17 (16.8)
Febuxostat	4 (4.0)
Antineoplastic and Immunomodulating Agents	16 (15.8)
Filgrastim	13 (12.9)

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Table 10.2.4.2-1: Concomitant Medications (Preferred Name Reported in ≥4% of Patients) - Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name[a]	Total (N=101)
Systemic Hormonal Preparations, excl. Sex Hormones and Insulins	13 (12.9)
Prednisone	5 (5.0)

[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.

Abbreviations: ATC, Anatomical Therapeutical Chemical (Classification System).

Concomitant medications are defined as medications other than study medications which are taken at any time on-treatment, ie, on or after the first day of study treatment and before the date of treatment discontinuation. Medications not in the WHO drug dictionary are classified as 'Not Coded'.

Medications taken for MCL are excluded.

Source: Table 14.1.10

10.2.5 Treatment Exposure and Dose Modification

Exposure to lenalidomide is summarised in Table 10.2.5-1.

The median lenalidomide treatment duration was 22.0 weeks (min: 0.4, max: 28.4). The median cumulative dose (sum of all doses taken across the treatment period) was 1340.0 mg (min: 20.0, max: 3800.0).

Lenalidomide dose reduction/interruption was reported in 84.2% of patients. The reason for dose reduction/interruption was AE in 47.5%, rest period in 28.7%, progressive disease in 20.8%, investigator decision in 12.9%, and other in 21.8% of patients. The median time to first dose reduction/interruption was 29.0 days (min: 3, max: 169). The median time to first dose reduction/interruption due to an AE was 29.5 days (min: 3, max: 172).

Information on treatment exposure is provided by patient in Appendix 1.7, Listing 16.2.5.1. Treatment doses of MCL therapies are provided by patient in Appendix 1.7, Listing 16.2.5.2.

Table 10.2.5-1: Treatment Exposure - Per Protocol Analysis Set

Parameter	Total (N=101)
Treatment Duration (weeks)[a]	
n (missing)	101 (0)
Mean	17.41
SD	10.086
Median	22.00
Q1, Q3	7.00, 26.14
Min, Max	0.4, 28.4
Cumulative Dose (mg)[b]	

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Table 10.2.5-1: Treatment Exposure - Per Protocol Analysis Set

Parameter	Total (N=101)
n (missing)	101 (0)
Mean	1564.06
SD	1096.915
Median	1340.00
Q1, Q3	570.00, 2430.00
Min, Max	20.0, 3800.0
Patients with Lenalidomide dose Reduction/Interruption, n (%)	85 (84.2)
Reason for Dose Reduction/Interruption, n (%)	
Adverse Event	48 (47.5)
Investigator Decision	13 (12.9)
Progressive disease	21 (20.8)
Rest Period	29 (28.7)
Other[c]	22 (21.8)
Time to First Dose Reduction/Interruption (days)[d]	
n (missing)	85 (0)
Mean	43.9
SD	40.31
Median	29.0
Q1, Q3	15.0, 57.0
Min, Max	3, 169
Time to First Dose Reduction/Interruption due to an AE (days)[e]	
n (missing)	48 (0)
Mean	47.1
SD	46.25
Median	29.5
Q1, Q3	15.0, 57.0
Min, Max	3, 172

[a] Defined as (date of last lenalidomide dose - date of first lenalidomide dose + 1)/7 without considering interruptions.
[b] Cumulative dose, defined as the sum of all doses taken across the treatment period in mg.
[c] Other reason specified is described in Table 14.2.1a.
[d] Calculated based on the number of patients with any dose reduction/interruption.
[e] Calculated based on the number of patients with any dose reduction/interruption due to an AE.
Abbreviations: AE, Adverse Event; Max, Maximum; Min, Minimum; Q1, First quartile; Q3, Third quartile; SD, Standard deviation.
Source: Table 14.2.1

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10.3 OUTCOME DATA

All analyses were conducted on the PPAS (N=101). Analyses pertaining to the primary and secondary endpoints were also repeated on the SAS (N=103) as sensitivity analysis.

The primary and secondary results are presented in Section 10.4.

10.4 MAIN RESULTS

10.4.1 Primary Objective

The primary objective was to quantify and characterise the event of TFR by tumour burden (assessed based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting.

10.4.1.1 TFR Summary

TFR by tumour burden status at baseline is summarised for the PPAS in Table 10.4.1.1-1.

In the PPAS, 6 patients (5.9%) had at least one TFR: 1 patient (2.1%) with low tumour burden at baseline, 2 patients (13.3%) with high tumour burden at baseline, and 3 patients (7.9%) with unknown tumour burden (referred to as 'other') at baseline. All of the patients had at least one TFR suspected to be related to lenalidomide.

Two patients (2.0%) had at least one serious TFR (1 patient [6.7%] with high tumour burden at baseline and 1 patient [2.6%] with unknown tumour burden at baseline).

Serious TFR reported in the patient with high tumour burden at baseline led to patient's death.

No patients experienced TFR leading to permanent lenalidomide discontinuation.

Overall, the median time to TFR onset was 16.0 days (min: 5, max: 169) and the median duration of TFR was 11.5 days (min: 1, max: 21).

TFR by tumour burden status at baseline is provided for the SAS in Appendix 1.6, Table 14.2.8.2.

Information on TFR and survival status is provided by patient in Appendix 1.7, Listing 16.2.6.1.

Table 10.4.1.1-1: TFR Summary by Tumour Burden Status at Baseline - Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other[a] (N=38)	Total (N=101)
Patients with at Least One TFR	1 (2.1)	2 (13.3)	3 (7.9)	6 (5.9)
Patients with at Least One TFR Suspected Related to Study Drug	1 (2.1)	2 (13.3)	3 (7.9)	6 (5.9)
Patients with at Least One Serious TFR	0	1 (6.7)	1 (2.6)	2 (2.0)
Patients with at Least One Serious TFR Suspected Related to Study Drug	0	1 (6.7)	1 (2.6)	2 (2.0)

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Table 10.4.1.1-1: TFR Summary by Tumour Burden Status at Baseline - Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other[a] (N=38)	Total (N=101)
Patients with at Least One CTCAE Grade 3/4[b] TFR	0	0	1 (2.6)	1 (1.0)
Patients with at Least One CTCAE Grade 3/4[b] TFR Suspected Related to Study Drug	0	0	1 (2.6)	1 (1.0)
Patients with at Least One TFR Leading to Death	0	1 (6.7)	0	1 (1.0)
Patients with at Least One TFR Suspected Related to Study Drug Leading to Death	0	1 (6.7)	0	1 (1.0)
Patients with at Least One TFR Leading to Permanent Study Drug Discontinuation	0	0	0	0
Patients with at Least One TFR Suspected Related to Study Drug Leading to Permanent Study Drug Discontinuation	0	0	0	0
Time to TFR Onset (days)				
n (missing)	1 (0)	2 (0)	3 (0)	6 (0)
Mean	10.0	88.5	44.3	53.3
SD	-	113.84	54.08	68.42
Median	10.0	88.5	22.0	16.0
Q1, Q3	10.0, 10.0	8.0, 169.0	5.0, 106.0	8.0, 106.0
Min, Max	10, 10	8, 169	5, 106	5, 169
Duration of TFR (days)[c]				
n (missing)	1 (0)	2 (0)	3 (0)	6 (0)
Mean	13.0	11.0	8.7	10.2
SD	-	14.14	7.09	7.96
Median	13.0	11.0	10.0	11.5
Q1, Q3	13.0, 13.0	1.0, 21.0	1.0, 15.0	1.0, 15.0
Min, Max	13, 13	1, 21	1, 15	1, 21

[a] Patients whose High Tumour Burden status was not documented in the medical charts were categorised as the 'Other' group.

[b] Graded using CTCAE version 3.0. Grade 3/4 and grade 5 are mutually exclusive.

[c] Defined as (date of TFR resolution - date of TFR onset+ 1).

Abbreviations: CTCAE, Common Terminology Criteria for Adverse Events; Max, Maximum; Min, Minimum; Q1, First quartile; Q3, Third quartile; SD, Standard deviation; TFR, Tumour flare reaction.

Patients are counted once per category.

Source: Table 14.2.8.1

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10.4.1.2 Incidence of TFR by Tumour Burden Status

Incidence of TFR by tumour burden status at baseline is summarised for the PPAS in Table 10.4.1.2-1.

In the PPAS, 6 patients had at least one TFR (1 patient with low tumour burden at baseline, 2 patients with high tumour burden at baseline, and 3 patients with unknown tumour burden (referred to as 'other') at baseline).

The cumulative incidence, ie, incidence proportion, of TFR over the study period was 5.9% (95% CI: 2.2%, 12.5%) overall, and 2.1% (95% CI: 0.1%, 11.1%) in patients with low tumour burden at baseline, 13.3% (95% CI: 1.7%, 40.5%) in patients with high tumour burden at baseline, and 7.9% (95% CI: 1.7%, 21.4%) in patients with unknown tumour burden at baseline.

The incidence rate of TFR was 14.4 per 100 PY (95% CI: 6.5, 32.1) overall and 4.7 per 100 PY (95% CI: 0.7, 33.3) among patients with low tumour burden at baseline, 34.2 per 100 PY (95% CI: 8.5, 136.6) among patients with high tumour burden at baseline, and 20.9 per 100 PY (95% CI: 6.7, 64.7) among patients with unknown tumour burden at baseline.

Incidence of TFR by tumour burden status at baseline is provided for the SAS in Appendix 1.6, Table 14.2.2.2.

Table 10.4.1.2-1: Incidence of TFR by Tumour Burden Status at Baseline - Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other [a] (N=38)	Total (N=101)
Number of Patients with at Least one TFR	1	2	3	6
Cumulative Incidence of TFR %	2.1	13.3	7.9	5.9
[95% CI][b]	(0.1, 11.1)	(1.7, 40.5)	(1.7, 21.4)	(2.2, 12.5)
Incidence Rate of TFR per 100 Person-Years, %	4.7	34.2	20.9	14.4
[95% CI][c]	(0.7, 33.3)	(8.5, 136.6)	(6.7, 64.7)	(6.5, 32.1)

[a] Patients whose High Tumour Burden status was not documented in the medical charts were categorised as the 'Other' group.

[b] Clopper-Pearson is used to calculate 95% CI.

[c] 95% CI for IR per 100 person-years is calculated using the method by RG Miller: IR*exp{+/- 1.96/square root of n}.

Abbreviations: CI, Confidence interval; IR, Incidence rate; TFR, Tumour flare reaction.

Source: Table 14.2.2.1

10.4.1.3 Time to TFR Onset by Tumour Burden Status

Time to TFR onset by tumour burden status at baseline is summarised for the PPAS in Table 10.4.1.3-1.

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The median follow-up duration was 6.0 months overall and in the three tumour burden subgroups.

The median time to TFR onset based on Kaplan-Meier estimates was not reached overall and in the three tumour burden subgroups.

Overall, the probability of TFR-free survival at 28 days was 96.0% (95% CI: 89.7%, 98.5%). The probability of TFR-free survival at 28 days was 97.9% (95% CI: 86.1%, 99.7%) in patients with low tumour burden at baseline, 93.3% (95% CI: 61.3%, 99.0%) in patients with high tumour burden at baseline, and 94.6% (95% CI: 80.0%, 98.6%) in patients with unknown tumour burden (referred to as 'other') at baseline.

There were no differences in the probability of TFR-free survival at 28, 56, and 84 days.

The probability of TFR-free survival at 6 months was 93.4% (95% CI: 85.9%, 97.0%) overall, 97.9% (95% CI: 86.1%, 99.7%) in patients with low tumour burden at baseline, 84.8% (95% CI: 51.2%, 96.0%) in patients with high tumour burden at baseline, and 90.9% (95% CI: 74.1%, 97.0%) in patients with unknown tumour burden at baseline.

Time to TFR onset by tumour burden status at baseline is provided for the SAS in Appendix 1.6, Table 14.2.3.2.

Table 10.4.1.3-1: Summary of Time to TFR Onset by Tumour Burden Status at Baseline - Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other[a] (N=38)	Total (N=101)
TFR-Free Survival, N				
n (missing)	48 (0)	15 (0)	38 (0)	101 (0)
Censored n (%)	47 (97.9)	13 (86.7)	35 (92.1)	95 (94.1)
Events n (%)	1 (2.1)	2 (13.3)	3 (7.9)	6 (5.9)
Median Time to TFR Onset[b] (months)	NR	NR	NR	NR
Two-sided 95% CI[c]	(NR, NR)	(NR, NR)	(NR, NR)	(NR, NR)
Timepoints TFR-Free Survival Probability[d]				
28 Days (Cycle 1) (95% CI)	97.9 (86.1, 99.7)	93.3 (61.3, 99.0)	94.6 (80.0, 98.6)	96.0 (89.7, 98.5)
56 Days (Cycle 2) (95% CI)	97.9 (86.1, 99.7)	93.3 (61.3, 99.0)	94.6 (80.0, 98.6)	96.0 (89.7, 98.5)
84 Days (Cycle 3) (95% CI)	97.9 (86.1, 99.7)	93.3 (61.3, 99.0)	94.6 (80.0, 98.6)	96.0 (89.7, 98.5)
6 Months Estimate (95% CI)	97.9 (86.1, 99.7)	84.8 (51.2, 96.0)	90.9 (74.1, 97.0)	93.4 (85.9, 97.0)
Follow-up Duration (months)				
n	48	15	38	101
Mean[e]	5.33	4.68	4.54	4.94
SD	1.554	2.285	2.008	1.871

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Table 10.4.1.3-1: Summary of Time to TFR Onset by Tumour Burden Status at Baseline - Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other[a] (N=38)	Total (N=101)
Median[e]	6.03	6.01	6.02	6.03
Q1, Q3	5.95, 6.03	2.66, 6.03	3.02, 6.03	4.24, 6.03
Min, Max	0.33, 6.03	0.26, 6.03	0.16, 6.03	0.16, 6.03

[a] Patients whose High Tumour Burden status was not documented in the medical charts were categorised as the 'Other' group.

[b] Median is based on Kaplan-Meier estimates.

[c] Two-sided Confidence interval based on the Kaplan-Meier estimates.

[d] Probability based on Kaplan-Meier estimates.

[e] The mean and median are the univariable statistics without adjusting for censoring.

Abbreviations: CI, Confidence Interval; Max, Maximum; Min, Minimum; NC, Not calculable; NR, Not reached; Q1, First quartile; Q3, Third quartile; SD, Standard deviation; TFR, Tumour flare reaction.

The time to TFR is defined as (TFR onset date - date of first Lenalidomide dose date + 1)/30.4375. Patients reporting no TFR are censored at the date of last information available within the 6-month period. Death related to a TFR event is considered as an event. Death unrelated to TFR is considered as a censoring event. All times to event are censored at 6 months after the first Lenalidomide dose date.

Source: Table 14.2.3.1

10.4.2 Secondary Objectives

The secondary objective was to quantify and characterise the proportion of early deaths (defined as deaths within 20 weeks of initial administration of lenalidomide) by tumour burden in R/R MCL patients treated with lenalidomide in a real-world setting.

10.4.2.1 Incidence of Early Death by Tumour Burden Status

Incidence of early death by tumour burden status at baseline is summarised for the PPAS in Table 10.4.2.1-1.

In the PPAS, early death was reported for 20 patients (6 patients with low tumour burden at baseline, 3 patients with high tumour burden at baseline, and 11 patients with unknown tumour burden [referred to as 'other'] at baseline).

The cumulative incidence of early death over the study period was 19.8% (95% CI: 12.5%, 28.9%) overall and 12.5% (95% CI: 4.7%, 25.2%) in patients with low tumour burden at baseline, 20.0% (95% CI: 4.3%, 48.1%) in patients with high tumour burden at baseline, and 28.9% (95% CI: 15.4%, 45.9%) in patients with unknown tumour burden at baseline.

The incidence rate of early death was 57.8 per 100 PY (95% CI: 37.3, 89.6) overall and 34.9 per 100 PY (95% CI: 15.7, 77.7) among patients with low tumour burden at baseline, 61.5 per 100 PY (95% CI: 19.8, 190.7) among patients with high tumour burden at baseline, and 87.6 per 100 PY (95% CI: 48.5, 158.2) among patients with unknown tumour burden at baseline.

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Incidence of early death by tumour burden status at baseline is provided for the SAS in Appendix 1.6, Table 14.2.4.2.

Table 10.4.2.1-1: Incidence of Early Death by Tumour Burden Status at Baseline - Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other[a] (N=38)	Total (N=101)
Number of Early Deaths	6	3	11	20
Cumulative Incidence of Early Death[b] %	12.5	20.0	28.9	19.8
[95% CI][c] %	(4.7, 25.2)	(4.3, 48.1)	(15.4, 45.9)	(12.5, 28.9)
Incidence Rate of Early Death per 100 Person-Years, %	34.9	61.5	87.6	57.8
95% CI[d]	(15.7, 77.7)	(19.8, 190.7)	(48.5, 158.2)	(37.3, 89.6)

[a] Patients whose High Tumour Burden status was not documented in the medical charts were categorised as the 'Other' group.
[b] Defined as death occurring within 20 weeks of the initial administration of lenalidomide.
[c] Clopper-Pearson is used to calculate 95% CI.
[d] 95% CI for IR per 100 person-years is calculated using the method by RG Miller: IR*exp{±1.96/square root of n}.
Abbreviations: CI, Confidence Interval; IR, Incidence rate.
Source: Table 14.2.4.1

10.4.2.2 Time to Early Death by Tumour Burden Status

Time to early death by tumour burden status at baseline is summarised for the PPAS in Table 10.4.2.2-1.

The median time to early death based on Kaplan-Meier estimates was not reached overall and in three tumour burden subgroups.

Overall, the probability of early death-free survival was 97.0% (95% CI: 91.1%, 99.0%) at 1 month, 92.1% (95% CI: 84.8%, 96.0%) at 2 months, 87.1% (95% CI: 78.8%, 92.3%) at 3 months, and 80.0% (95% CI: 70.7%, 86.6%) at 20 weeks.

In patients with low tumour burden at baseline, the probability of early death-free survival was 100.0 (95% CI not calculable) at 1 month, 93.7% (95% CI: 81.9%, 97.9%) at 2 months , 91.6% (95% CI: 79.2%, 96.8%) at 3 months, and 87.4% (95% CI: 74.0%, 94.1%) at 20 weeks.

In patients with high tumour burden at baseline, the probability of early death-free survival was 93.3% (95% CI: 61.3%, 99.0%) at 1 month, 86.7% (95% CI: 56.4%, 96.5%) at 2 months, 80.0% (95% CI: 50.0%, 93.1%) at 3 months, and 80.0% (95% CI not calculable) at 20 weeks.

In patients with unknown tumour burden (referred to as ‘other’) at baseline, the probability of early death-free survival was 94.7% (95% CI: 80.6%, 98.7%) at 1 month, 92.1% (95% CI: 77.5%,

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97.4%) at 2 months, 84.2% (95% CI: 68.2%, 92.6%) at 3 months, and 70.8% (95% CI: 53.5%, 82.6%) at 20 weeks.

Time to early death by tumour burden status at baseline is provided for the SAS in Appendix 1.6, Table 14.2.5.2.

Table 10.4.2.2-1: Summary of Time to Early Death by Tumour Burden Status at Baseline - Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other[a] (N=38)	Total (N=101)
Early Death Free Survival, N				
n (%)	48 (100.0)	15 (100.0)	38 (100.0)	101 (100.0)
Censored n (%)	42 (87.5)	12 (80.0)	27 (71.1)	81 (80.2)
Events n (%)	6 (12.5)	3 (20.0)	11 (28.9)	20 (19.8)
Median Time to Early Death[b] (months)	NR	NR	NR	NR
Two-sided 95% CI[c]	(NR, NR)	(2.7, NR)	(NR, NR)	(NR, NR)
Timepoints Early Death Free Survival Probability[d]				
1 Month Estimate (95% CI)	100.0 (NC, NC)	93.3 (61.3, 99.0)	94.7 (80.6, 98.7)	97.0 (91.1, 99.0)
2 Month Estimate (95% CI)	93.7 (81.9, 97.9)	86.7 (56.4, 96.5)	92.1 (77.5, 97.4)	92.1 (84.8, 96.0)
3 Month Estimate (95% CI)	91.6 (79.2, 96.8)	80.0 (50.0, 93.1)	84.2 (68.2, 92.6)	87.1 (78.8, 92.3)
Week 20th Estimate (95% CI)	87.4 (74.0, 94.1)	80.0 (NC, NC)	70.8 (53.5, 82.6)	80.0 (70.7, 86.6)
Follow-up Duration (months)				
n	48	15	38	101
Mean[e]	4.30	3.90	3.96	4.11
SD	0.908	1.404	1.192	1.104
Median[e]	4.63	4.63	4.63	4.63
Q1, Q3	4.63, 4.63	3.35, 4.63	3.06, 4.63	4.63, 4.63
Min, Max	1.2, 4.6	0.3, 4.6	0.4, 4.6	0.3, 4.6

[a] Patients whose High Tumour Burden status was not documented in the medical charts were categorised as the 'Other' group.

[b] Median is based on Kaplan-Meier estimates.

[c] Two-sided Confidence interval based on the Kaplan-Meier estimates.

[d] Probability based on Kaplan-Meier estimates.

[e] The mean and median are the univariable statistics without adjusting for censoring.

Abbreviations: CI, Confidence interval, Max, Maximum; Min, Minimum; NA, Not Applicable; NC, Not calculable; NR, Not reached; Q1, First quartile; Q3, Third quartile; SD, Standard deviation.

The time to Early Death is defined as (Death date - date of first Lenalidomide dose date + 1)/30.4375. All times to event are censored at 20 weeks after the first Lenalidomide dose date.

Source: Table 14.2.5.1

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10.4.3 Other Analyses

10.4.3.1 Best Response During Lenalidomide Therapy

Best response during lenalidomide therapy is summarised for the PPAS in Table 10.4.3.1-1.

Best response during lenalidomide therapy was assessed in 39 patients (38.6%). Best response was complete response in 12 patients (30.8%), partial response in 16 patients (41.0%), and stable disease in 6 patients (15.4%).

Information on best response during lenalidomide therapy is provided by patient in Appendix 1.7, Listing 16.2.6.2.

Table 10.4.3.1-1: Best Response During Lenalidomide Therapy - Per Protocol Analysis Set

Parameter	Total (N=101) n (%)
Patients with Best Response Assessment Performed	39 (38.6)
Best Response During Lenalidomide Therapy[a]	
Complete Response	12 (30.8)
Partial Response	16 (41.0)
Stable Disease	6 (15.4)
Progressive Disease	5 (12.8)
Not Evaluable	0 (0.0%)
Unknown	0 (0.0%)
Method of response assessment[a]	
CT Scan	18 (46.2)
MRI	1 (2.6)
OTHER	1 (2.6)
PET/CT Scan	11 (28.2)
Unknown	8 (20.5)

[a] Percentages are calculated using the number of patients who performed the best response assessment.
Abbreviations: CT, Computed tomography; MRI, Magnetic resonance imaging; PET, Positron emission tomography.
Source: Table 14.3.1.1

10.4.3.2 Exploration of Risk Factors Associated with TFR

Results of the multivariable analysis using Cox regression on TFR are summarised for the PPAS in Table 10.4.3.2-1.

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The results of the univariable Cox analysis showed a significant association between the occurrence of TFR and age: the risk of TFR was 5.76 times greater in patients aged <65 years vs. patients aged ≥65 years (HR: 5.76 [95% CI: 1.16, 28.57], p=0.0320). However, no covariates were retained for the multivariable Cox analysis. After adjusting for the other covariates in the model, age was no longer significant, as represented in the multivariable Cox analysis.

Table 10.4.3.2-1: Summary of Multivariable Analysis Using Cox Regression on TFR - Per Protocol Analysis Set

	Univariable Analysis			Multivariable Analysis[a]		
Baseline Risk Factor	**Hazard Ratio**	**[95% CI]**	**p-value**	**Hazard Ratio**	**[95% CI]**	**p-value**
Age Group (<65 vs >=65)	5.76	(1.16, 28.57)	0.0320	-	-	-
Sex (Female vs Male)	4.45	(0.89, 22.16)	0.0685	-	-	-
History of TFR (Yes vs No)	3.89	(0.45, 33.54)	0.2170	-	-	-
Tumour Burden at Baseline (High vs Low)	6.89	(0.62, 76.05)	0.1152	-	-	-
Bulky Disease at Baseline (Yes vs No)	1.49	(0.16, 14.33)	0.7296	-	-	-
ECOG Performance Status			0.7327			-
(1 vs 0)	0.43	(0.04, 4.13)		-	-	
(2+ vs 0)	1.12	(0.12, 10.81)		-	-	

[a] No variables have been retained for the multivariable analysis.
Abbreviations: CI, Confidence interval; ECOG, Eastern Cooperative Oncology Group; TFR, Tumour flare reaction.

References: Age Group = >=65 Years; Sex = Male; History of TFR = No; Tumour Burden at Baseline = Low; Bulky Disease at Baseline = No; ECOG Performance Status = 0.

The time to Early Death is defined as (Death date – date of first Lenalidomide dose date + 1)/30.4375. All times to event are censored at 20 weeks after the first Lenalidomide dose date.

Variables with p-value <0.20 in the univariable analysis were selected for the multivariable. Final variables were selected using a backward elimination variable-selection procedure with an elimination criterion >0.10.

Source: Table 14.2.6

10.4.3.3 Exploration of Risk Factors Associated with Early Death

Results of the multivariable analysis using Cox regression on early death are summarised for the PPAS in Table 10.4.3.3-1.

No significant associations between the occurrence of early death and the pre-defined potential risk factors were found in the univariable or multivariable analyses.

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Table 10.4.3.3-1: Summary of Multivariable Analysis Using Cox Regression on Early Death - Per Protocol Analysis Set

	Univariable Analysis			Multivariable Analysis[a]		
Baseline Risk Factor	**Hazard Ratio**	**[95% CI]**	**p-value**	**Hazard Ratio**	**[95% CI]**	**p-value**
Age Group (<65 vs >=65)	0.59	(0.14, 2.54)	0.4764	-	-	-
Sex (Female vs Male)	2.19	(0.87, 5.49)	0.0948	-	-	-
History of TFR (Yes vs No)	0.91	(0.12, 6.78)	0.9244	-	-	-
Tumour Burden at Baseline (High vs Low)	1.73	(0.43, 6.93)	0.4373	-	-	-
Bulky Disease at Baseline (Yes vs No)	1.26	(0.35, 4.51)	0.7244	-	-	-
ECOG Performance Status			0.9434			-
(1 vs 0)	1.01	(0.27, 3.78)		-	-	
(2+ vs 0)	1.31	(0.25, 6.77)		-	-	

[a] No variables have been retained for the multivariable analysis.
Abbreviations: CI, Confidence interval; ECOG, Eastern Cooperative Oncology Group; TFR, Tumour flare reaction.

References: Age Group = >=65 Years; Sex = Male; History of TFR = No; Tumour Burden at Baseline = Low; Bulky Disease at Baseline = No; ECOG Performance Status = 0.

The time to Early Death is defined as (Death date– date of first Lenalidomide dose date + 1)/30.4375. All times to event are censored at 20 weeks after the first Lenalidomide dose date.

Variables with p-value <0.20 in the univariable analysis were selected for the Multivariable. Final variables were selected using a backward elimination variable-selection procedure with an elimination criterion >0.10.

Source: Table 14.2.7

10.5 ADVERSE EVENTS/ADVERSE REACTIONS

10.5.1 Adverse Events

10.5.1.1 AE Summary

TEAEs related to lenalidomide and not listed in the current EU SmPC (Version 58.0 approved on 09-Feb-2023) ("related AEs") are provided for the PPAS in Table 10.5.1.1-1.

In the PPAS, 10 patients (9.9%) experienced at least one related AE and grade 3/4 related AEs were reported in 5 patients (5.0%).

Related SAEs were reported in 4 patients (4.0%).

Related AEs leading to death were reported in 3 patients (3.0%).

Related AEs leading to permanent lenalidomide discontinuation were reported in 2 patients (2.0%).

TEAEs related to lenalidomide and not listed in current EU SmPC are provided for the SAS in Appendix 1.6, Table 14.3.2.1.2.

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AEs were reported in the SAS were the same as those reported in the PPAS.

Table 10.5.1.1-1: Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC Summary - Per Protocol Analysis Set

TEAE Categories	Total (N=101) n (%)
Patients with at Least One Related AE	10 (9.9)
Patients with at Least One Serious Related AE	4 (4.0)
Patients with at Least One CTCAE Grade 3/4[a] Related AE	5 (5.0)
Patients with at Least One Related AE Leading to Death	3 (3.0)
Patients with at Least One Related AE Leading to Permanent Study Drug Discontinuation	2 (2.0)

[a] Graded using CTCAE version 5.0. Grade 3/4 and grade 5 are mutually exclusive.
Abbreviations: AE, Adverse event; CTCAE, Common Terminology Criteria for Adverse Events; EU, European Union; SmPC, Summary of Product Characteristics; TEAE, Treatment-emergent adverse event.
Patients are counted once per category.
Source: Table 14.3.2.1.1

10.5.1.2 AEs Related to Lenalidomide and Not Listed in Current EU SmPC

AEs related to lenalidomide and not listed in the current EU SmPC are presented for the PPAS in Table 10.5.1.2-1.

Each reported AE related to lenalidomide and not listed in the current EU SmPC was experienced by a single patient.

AEs related to lenalidomide and not listed in the current EU SmPC in the SAS were the same as those reported in the PPAS (Appendix 1.6, Table 14.3.2.2.2).

AEs related to lenalidomide and not listed in the current EU SmPC are provided by patient in Appendix 1.7, Listing 16.2.7.1.

Table 10.5.1.2-1: AEs Related to Lenalidomide and Not Listed in Current EU SmPC by System Organ Class and Preferred Term - Per Protocol Analysis Set

System Organ Class Preferred Term[a]	Total (N=101) n (%)
Patients With at Least One Related AE	10 (9.9)
Blood and Lymphatic System Disorders	**3 (3.0)**
Immune Thrombocytopenia	1 (1.0)
Lymphadenopathy	1 (1.0)

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Table 10.5.1.2-1: AEs Related to Lenalidomide and Not Listed in Current EU SmPC by System Organ Class and Preferred Term - Per Protocol Analysis Set

System Organ Class Preferred Term[a]	Total (N=101) n (%)
Lymphocytosis	1 (1.0)
General Disorders and Administration Site Conditions	**2 (2.0)**
Death	1 (1.0)
General Physical Health Deterioration	1 (1.0)
Immune System Disorders	**2 (2.0)**
Graft Versus Host Disease in Gastrointestinal Tract	1 (1.0)
Graft Versus Host Disease in Skin	1 (1.0)
Haemophagocytic Lymphohistiocytosis	1 (1.0)
Nervous System Disorders	**2 (2.0)**
Encephalopathy	1 (1.0)
Presyncope	1 (1.0)
Hepatobiliary Disorders	**1 (1.0)**
Venoocclusive Liver Disease	1 (1.0)
Investigations	**1 (1.0)**
Glomerular Filtration Rate Decreased	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary are classified as 'Not Coded'.
Abbreviations: AE, Adverse event; EU, European Union; SmPC, Summary of Product Characteristics.
Source: Table 14.3.2.2.1

10.5.1.3 Grade 3/4 AEs Related to Lenalidomide and Not Listed in Current EU SmPC

Grade 3/4 AEs related to lenalidomide and not listed in the current EU SmPC are presented for the PPAS in Table 10.5.1.3-1.

Grade 3/4 AEs related to lenalidomide and not listed in the current EU SmPC consisted of encephalopathy, glomerular filtration rate decreased, haemophagocytic lymphohistiocytosis, immune thrombocytopenia, and presyncope (1 patient each).

Grade 3/4 AEs related to lenalidomide and not listed in the current EU SmPC are provided for the SAS in Appendix 1.6, Table 14.3.2.4.2.

Grade 3/4 AEs related to lenalidomide and not listed in the current EU SmPC are provided by patient in Appendix 1.7, Listing 16.2.7.2.

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Table 10.5.1.3-1: Grade 3/4 AEs Related to Lenalidomide and Not Listed in Current EU SmPC by System Organ Class and Preferred Term - Per Protocol Analysis Set

System Organ Class Preferred Term[a]	Total (N=101) n (%)
Patients With at Least One Grade 3/4 Related AE	5 (5.0)
Nervous System Disorders	**2 (2.0)**
Encephalopathy	1 (1.0)
Presyncope	1 (1.0)
Blood and Lymphatic System Disorders	**1 (1.0)**
Immune Thrombocytopenia	1 (1.0)
Immune System Disorders	**1 (1.0)**
Haemophagocytic Lymphohistiocytosis	1 (1.0)
Investigations	**1 (1.0)**
Glomerular Filtration Rate Decreased	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary are classified as 'Not Coded'.
Abbreviations: AE, Adverse event; EU, European Union; SmPC, Summary of Product Characteristics.
Source: Table 14.3.2.4.1

10.5.1.4 SAEs Related to Lenalidomide and Not Listed in Current EU SmPC

SAEs related to lenalidomide and not listed in the current EU SmPC are presented for the PPAS in Table 10.5.1.4-1.

SAEs related to lenalidomide and not listed in the current EU SmPC consisted of death, encephalopathy, general physical health deterioration, immune thrombocytopenia, and venoocclusive liver disease.

SAEs related to lenalidomide and not listed in the current EU SmPC are provided for the SAS in Appendix 1.6, Table 14.3.2.3.2.

SAEs not listed in the current EU SmPC are provided by patient in Appendix 1.7, Listing 16.2.7.3.

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Table 10.5.1.4-1: SAEs Related to Lenalidomide and Not Listed in Current EU SmPC by System Organ Class and Preferred Term - Per Protocol Analysis Set

System Organ Class Preferred Term[a]	Total (N=101) n (%)
Patients With at Least One Serious Related AE	4 (4.0)
General Disorders and Administration Site Conditions	**2 (2.0)**
Death	1 (1.0)
General Physical Health Deterioration	1 (1.0)
Blood and Lymphatic System Disorders	**1 (1.0)**
Immune Thrombocytopenia	1 (1.0)
Hepatobiliary Disorders	**1 (1.0)**
Venoocclusive Liver Disease	1 (1.0)
Nervous System Disorders	**1 (1.0)**
Encephalopathy	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary are classified as 'Not Coded'.
Abbreviations: AE, Adverse event; EU, European Union; SmPC, Summary of Product Characteristics.
Source: Table 14.3.2.3.1

10.5.1.5 Deaths

10.5.1.5.1 AEs Related to Lenalidomide Leading to Death and Not Listed in Current EU SmPC

AEs related to lenalidomide leading to death and not listed in the current EU SmPC are presented for the PPAS in Table 10.5.1.5-1.

Reported AEs related to lenalidomide leading to death and not listed in the current EU SmPC consisted of death, general physical health deterioration, and venoocclusive liver disease (1 patient each).

AEs related to lenalidomide leading to death and not listed in the current EU SmPC are provided for the SAS in Appendix 1.6, Table 14.3.2.5.2.

AEs related to lenalidomide leading to death and not listed in the current EU SmPC are provided by patient in Appendix 1.7, Listing 16.2.7.4.

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Table 10.5.1.5-1: AEs Related to Lenalidomide Leading to Death and Not Listed in Current EU SmPC by System Organ Class and Preferred Term - Per Protocol Analysis Set

System Organ Class Preferred Term[a]	Total (N=101) n (%)
Patients With at Least One Related AE Leading to Death	3 (3.0)
General Disorders and Administration Site Conditions	**2 (2.0)**
Death	1 (1.0)
General Physical Health Deterioration	1 (1.0)
Hepatobiliary Disorders	**1 (1.0)**
Venoocclusive Liver Disease	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary are classified as 'Not Coded'.
Abbreviations: AE, Adverse event; EU, European Union; SmPC, Summary of Product Characteristics.
Source: Table 14.3.2.5.1

10.5.1.5.2 Death Summary

Information on deaths is summarised for the PPAS in Table 10.5.1.5-2.

Overall, 26 deaths (25.7%) were reported, including 7 deaths on treatment (6.9%). The most frequent primary causes of death reported were mantle cell lymphoma (8 patients [30.8%]), death (5 patients [19.2%]), general physical health deterioration (2 patients [7.7%]), and non-Hodgkin's lymphoma 2 patients [7.7%]).

The primary causes of death on treatment were mantle cell lymphoma (3 patients [42.9%]), atrioventricular block complete (1 patient [14.3%]), myocardial ischaemia (1 patient [14.3%]), pneumonia bacterial (1 patient [14.3%]), and urosepsis (1 patient [14.3%]).

Table 10.5.1.5-2: Death Summary - Per Protocol Analysis Set

Parameter	Total (N=101) n (%)
Overall Number of Deaths	26 (25.7)
Primary Cause of Death	
Atrioventricular Block Complete	1 (3.8)
Death	5 (19.2)
General Physical Health Deterioration	2 (7.7)
Mantle Cell Lymphoma	8 (30.8)

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Table 10.5.1.5-2: Death Summary - Per Protocol Analysis Set

Parameter	Total (N=101) n (%)
Mantle Cell Lymphoma Recurrent	1 (3.8)
Multiple Organ Dysfunction Syndrome	1 (3.8)
Myocardial Ischaemia	1 (3.8)
Non-Hodgkin's Lymphoma	2 (7.7)
Pneumonia Bacterial	1 (3.8)
Respiratory Failure	1 (3.8)
Sepsis	1 (3.8)
Urosepsis	1 (3.8)
Venoocclusive Liver Disease	1 (3.8)
Number of Deaths on Treatment[a]	7 (6.9)
Primary Cause of Death on Treatment	
Atrioventricular Block Complete	1 (14.3)
Mantle Cell Lymphoma	3 (42.9)
Myocardial Ischaemia	1 (14.3)
Pneumonia Bacterial	1 (14.3)
Urosepsis	1 (14.3)

[a] On treatment death is defined as a death occurring either during the course of treatment or within 28 days following the discontinuation of treatment.
Source: Table 14.3.3.1

10.5.1.5.3 Early Death Summary

Information on early deaths is summarised for the PPAS in Table 10.5.1.5-3.

Overall, 20 early deaths were reported (19.8%). The most frequent primary causes of early death reported were mantle cell lymphoma (7 patients [35.0%]), death (3 patients [15.0%]), and general physical health deterioration (2 patients [10.0%]).

Information on early deaths is provided for the SAS in Appendix 1.6, Table 14.3.3.2.2.

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Table 10.5.1.5-3: Early Death Summary - Per Protocol Analysis Set

Parameter	Total (N=101) n (%)
Overall Number of Early Deaths[a]	20 (19.8)
Primary Cause of Early Death	
Death	3 (15.0)
General Physical Health Deterioration	2 (10.0)
Mantle Cell Lymphoma	7 (35.0)
Mantle Cell Lymphoma Recurrent	1 (5.0)
Multiple Organ Dysfunction Syndrome	1 (5.0)
Myocardial Ischaemia	1 (5.0)
Non-Hodgkin's Lymphoma	1 (5.0)
Pneumonia Bacterial	1 (5.0)
Respiratory Failure	1 (5.0)
Sepsis	1 (5.0)
Urosepsis	1 (5.0)

[a] Defined as death occurring within 20 weeks of the initial administration of lenalidomide.
Source: Table 14.3.3.2.1

10.5.1.6 AEs Related to Lenalidomide Leading to Permanent Study Drug Discontinuation and Not Listed in Current EU SmPC

AEs related to lenalidomide leading to permanent lenalidomide discontinuation and not listed in the current EU SmPC are presented for the PPAS in Table 10.5.1.6-1.

Reported AEs related to lenalidomide leading to permanent lenalidomide discontinuation and not listed in the current EU SmPC consisted of graft versus host disease in gastrointestinal tract and haemophagocytic lymphohistiocytosis (1 patient each).

AEs related to lenalidomide leading to permanent lenalidomide discontinuation and not listed in the current EU SmPC are provided for the SAS in Appendix 1.6, Table 14.3.2.6.2.

AEs leading to permanent lenalidomide discontinuation and not listed in the current EU SmPC are provided by patient in Appendix 1.7, Listing 16.2.7.5.

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Table 10.5.1.6-1: AEs Related to Lenalidomide Leading to Permanent Study Drug Discontinuation and Not Listed in Current EU SmPC by System Organ Class and Preferred Term - Per Protocol Analysis Set

System Organ Class Preferred Term[a]	Total (N=101) n (%)
Patients With at Least One Related AE Leading to Permanent Study Drug Discontinuation	2 (2.0)
Immune System Disorders	**2 (2.0)**
Graft Versus Host Disease in Gastrointestinal Tract	1 (1.0)
Haemophagocytic Lymphohistiocytosis	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary are classified as 'Not Coded'.
Abbreviations: AE, Adverse event; EU, European Union; SmPC, Summary of Product Characteristics.
Source: Table 14.3.2.6.1

10.5.2 Pregnancies

No information on pregnancy was collected as part of the study.

10.5.3 Physical Exam

Physical exam results are provided in Appendix 1.6, Table 14.3.4.1.1 (baseline) and Table 14.3.4.1.2 (by visit). Physical exam results are provided by patient in Appendix 1.7, Listing 16.2.8.1.

Abnormal findings from physical exam were observed in ≤2 patients at all visits, except abnormal lymph node at Visit 1 (3 patients).

10.5.4 Clinical Laboratory Evaluations

Haematology results by visit are provided in Appendix 1.6, Table 14.3.4.2.

Biochemistry chemistry results by visit are provided in Appendix 1.6, Table 14.3.4.3.

Laboratory data are provided by patient in Appendix 1.7, Listing 16.2.8.2.

11 DISCUSSION

11.1 KEY RESULTS

Analyses reflect patient data collected between 02-Oct-2018 (first patient enrolled) through 10-Jan-2024 (last patient last visit). Database lock was 20-Feb-2024.

A total of 105 patients were screened. Among these, 103 patients (98.1%) received at least one dose of treatment and were included in the SAS and 101 (96.2%) met the eligibility criteria to comprise the PPAS.

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As there was only a 2-patient difference between the PPAS and the SAS, the results in the PPAS and the results in the SAS (sensitivity analyses) were very similar.

In the PPAS, 71 patients (70.3%) completed the study and 30 (29.7%) discontinued the study. The reasons for study discontinuation consisted of death (26 patients) and lost to follow-up (4 patients).

In the PPAS, the median age was 74.0 years (min: 44, max: 91) and 79.2% of patients were male.

The median time from initial MCL diagnosis to start of lenalidomide was 51 months (min: 2, max: 207) and the median time from relapse/progression to start of lenalidomide was 0.85 months (min: 0.0, max: 114.3). The vast majority of patients received at least one previous line of therapy (55.4% had 1, 28.7% had 2, and 14.8% had ≥3 previous lines of therapy) and 24.8% of patients had prior stem cell transplant. The best response achieved prior to lenalidomide was complete response (73.5% of patients), partial response (16.3%), and stable disease (5.1%).

At baseline, low tumour burden was reported in 48 patients (47.5%) and high tumour burden in 15 patients (14.9%). Tumour burden was not documented in the medical charts for 38 patients (37.6%).

The median lenalidomide treatment duration was 22.0 weeks (min: 0.4, max: 28.4) with a median cumulative dose of lenalidomide of 1340.00 mg (min: 20.0, max: 3800.0).

11.1.1 Primary Objective

The primary objective was to quantify and characterise the event of TFR by tumour burden (assessed based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting.

In the PPAS, TFR events were reported in 6 patients (1 patient with low tumour burden at baseline, 2 patients with high tumour burden at baseline, and 3 patients with unknown tumour burden at baseline). Serious TFR was reported in 2 patients (2.0%) (1 patient with high tumour burden at baseline [fatal case] and 1 patient with unknown tumour burden at baseline). No patients experienced TFR leading to permanent lenalidomide discontinuation.

Overall, the cumulative incidence, ie, incidence proportion, of TFR was 5.9% (95% CI: 2.2%, 12.5%) over the study period and the incidence rate of TFR was 14.4 per 100 PY (95% CI: 6.5, 32.1).

The cumulative incidence of TFR was numerically greater in patients with high tumour burden at baseline compared to patients with low tumour burden at baseline (13.3% [95% CI: 1.7%, 40.5%] vs. 2.1% [95% CI: 0.1%, 11.1%], respectively). Similarly, the incidence rate of TFR was numerically greater in patients with high tumour burden at baseline than in patients with low tumour burden at baseline (34.2 per 100 PY [95% CI: 8.5, 136.6]) vs. 4.7 per 100 PY [95% CI: 0.7, 33.3], respectively), though the 95% CIs were wide.

Among patients with unknown tumour burden at baseline, the cumulative incidence of TFR was 7.9% (95% CI: 1.7%, 21.4%) and the incidence rate of TFR was 20.9 per 100 PY (95% CI: 6.7, 64.7).

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The median time to TFR onset based on Kaplan-Meier estimates was not reached overall and in the three tumour burden subgroups. Overall, the probability of TFR-free survival at 6 months was 93.4% (95% CI: 85.9%, 97.0%). The probability of TFR-free survival at 6 months was numerically lower in patients with high tumour burden at baseline than in patients with low tumour burden at baseline (84.8% [95% CI: 51.2%, 96.0%] vs. 97.9% [95% CI: 86.1%, 99.7%], respectively). The probability of TFR-free survival at 6 months was 90.9% (95% CI: 74.1%, 97.0%) in patients with unknown tumour burden at baseline.

11.1.2 Secondary Objectives

The secondary objective was to quantify and characterise the proportion of early deaths (defined as deaths within 20 weeks of initial administration of lenalidomide) by tumour burden in R/R MCL patients treated with lenalidomide in a real-world setting.

In the PPAS, early death was reported for 20 patients (6 patients with low tumour burden at baseline, 3 patients with high tumour burden at baseline, and 11 patients with unknown tumour burden at baseline). The primary cause of early death was related to the progression of the underlying disease.

Overall, the cumulative incidence of early death was 19.8% (95% CI: 12.5%, 28.9%) and the incidence rate of early death was 57.8 per 100 PY (95% CI: 37.3, 89.6).

The cumulative incidence of early death was numerically greater in patients with high tumour burden at baseline than in patients with low tumour burden at baseline (20.0% [95% CI: 4.3%, 48.1%] vs. 12.5% [95% CI: 4.7%, 25.2%]). The incidence rate of early death was also numerically greater in patients with high tumour burden at baseline than in patients with low tumour burden at baseline (61.5 per 100 PY [95% CI: 19.8, 190.7] vs. 34.9 per 100 PY [95% CI: 15.7, 77.7]), though the 95% CIs were wide.

Among patients with unknown tumour burden at baseline, the cumulative incidence of early death was 28.9% (95% CI: 15.4%, 45.9%) and the incidence rate of early death was 87.6 per 100 PY (95% CI: 48.5, 158.2).

The median time to early death based on Kaplan-Meier estimates was not reached overall and in three tumour burden subgroups.

The probability of early death-free survival at 20 weeks was numerically lower in patients with high tumour burden at baseline than in patients with low tumour burden at baseline (80.0% [95% CI not calculable] vs. 87.4% [95% CI: 74.0%, 94.1%], respectively). The probability of early death-free survival at 20 weeks was 70.8% (95% CI: 53.5%, 82.6%) in patients with unknown tumour burden at baseline.

11.1.3 Other Analyses

- Best response during lenalidomide therapy

In the PPAS, best response during lenalidomide therapy was assessed in 39 patients: 30.8% had a complete response, 41.0% had a partial response, and 15.4% had a stable disease.

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- Risk factors associated with TFR

Although age was initially associated with TFR risk in the univariable Cox analysis, after adjusting for other potential risk factors, the apparent association of age and TFR risk was no longer significant in the multivariable Cox analysis.

- Risk factors associated with early death

No significant associations between the occurrence of early death and the pre-defined potential risk factors were found.

11.1.4 Other Safety Results

Only TEAEs related to lenalidomide that were not reported in the current Revlimid EU SmPC ("related AE") were reported in this study.

Related AEs reported in the SAS were the same as those reported in the PPAS.

In the PPAS, related AEs were reported in 10 patients (9.9%) and related SAEs in 4 patients (4.0%). Related SAEs consisted of death, encephalopathy, general physical health deterioration, immune thrombocytopenia, and venoocclusive liver disease.

Related AEs leading to death were reported in 3 patients (3.0%) and consisted of death, general physical health deterioration, and venoocclusive liver disease.

Related AEs leading to permanent lenalidomide discontinuation were reported in 2 patients (2.0%) and consisted of graft versus host disease in gastrointestinal tract and haemophagocytic lymphohistiocytosis.

11.2 LIMITATIONS

This study presented the following limitations.

Due to the observational retrospective design of the study, there were missing data for several variables of interest. In particular, information on tumour burden was not documented in the medical charts for 37.6% of patients, reducing the statistical precision of the results in the high tumour burden and low tumour burden subgroups. For instance, among the 20 early deaths reported in this study, 11 occurred in patients with unknown tumour burden at baseline.

Since the study was designed with TFR as the main outcome, the sample size was too limited to provide a precise estimate for the related AEs. However, the AEs captured through the review of medical records were an improvement on spontaneous reporting as these events may not have been captured through normal channels.

In addition, the multivariable analysis performed to identify factors associated with TFR was conducted on a limited number of TFR events. Therefore, the results should be interpreted with caution.

11.2.1 Strengths of Research Methods

Despite the limitations mentioned above, this study provided meaningful information regarding lenalidomide safety profile in real-life management of patients with R/R MCL.

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11.3 INTERPRETATION

This study was conducted to further characterise potential safety events of TFR and early deaths by tumour burden, as well as other potential safety risks, in R/R MCL patients in a real-world setting.

In total, 101 patients received lenalidomide and met the eligibility criteria for the PPAS.

TFR events were reported in 6 patients (2 patients with high tumour burden at baseline, 1 patient with low tumour burden at baseline, and 3 patients with unknown tumour burden at baseline). Serious TFR was reported in 2 patients (2.0%) (1 patient with high tumour burden at baseline [fatal case] and 1 patient with unknown tumour burden at baseline). The cumulative incidence of TFR was 5.9% overall, 13.3% in patients with high tumour burden at baseline and 2.1% in patients with low tumour burden at baseline.

Overall, the proportion of patients in this study who experienced TFR was lower than that observed previously in clinical trials. In study MCL-002, 9.6% of lenalidomide-treated subjects (16/167) experienced TFR. Of these 16 subjects, 3 (1.8%) experienced Grade 3 or 4 TFR, including 1 subject (0.6%) who experienced serious TFR and 1 subject (0.6%) who experienced TFR resulting in treatment discontinuation.[4] In study MCL-001 (EMERGE), a multicentre Phase 2 study examining the safety and efficacy of lenalidomide in 134 subjects who had relapsed or were refractory to bortezomib, 9.7% of lenalidomide-treated subjects (13/134) experienced TFR events (Grade 1 to 2). No subjects discontinued lenalidomide therapy due to TFR.[17] In a Phase 2 study conducted in 38 subjects with MCL treated with lenalidomide in combination with rituximab and followed for 9 years, 14 subjects (36.8%) experienced TFR (4 subjects [10.5%] had Grade ≥3 TFR).[21,22]

In this observational study, early death was reported for 20 patients (3 patients with high tumour burden at baseline, 6 patients with low tumour burden at baseline, and 11 patients with unknown tumour burden at baseline). The cumulative incidence of early deaths was 20.0% (95% CI: 4.3%, 48.1%) in patients with high tumour burden at baseline, which was comparable with the results in clinical trial MCL-002 (19.8% [16/81]).[4] In the overall study population, the cumulative incidence of early deaths in this observational study was 19.8% (95% CI: 12.5%, 28.9%) and was greater than that observed in clinical trial MCL-002 (13.2% [22/167] in lenalidomide-treated subjects).

Overall, this study shows that the cumulative incidence of TFR and the cumulative incidence of early death in R/R MCL patients treated with lenalidomide in a real-world setting were consistent with what had been previously reported in the MCL lenalidomide clinical trials.

This study also collected information about AEs related to lenalidomide that were not reported in the current Revlimid EU SmPC.

Related AEs were reported in 10 patients (9.9%). Each related AE was reported in a single patient. Four (4) patients experienced related SAEs, including 3 patients who had related AEs leading to death (death, general physical health deterioration, and venoocclusive liver disease). Two (2) patients experienced related AEs leading to permanent lenalidomide discontinuation (graft versus host disease in gastrointestinal tract and haemophagocytic lymphohistiocytosis).

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The results of study CC-5013-MCL-005 suggest that there are no new safety concerns associated with lenalidomide treatment in R/R MCL patients that were not previously identified as part of the clinical development program.

11.4 GENERALIZABILITY

Participation in this study was open to all adult patients that received at least one dose of lenalidomide for the treatment of R/R MCL and did not participate in an interventional clinical trial during the treatment period under observation in this PASS. These broad inclusion and exclusion criteria aimed to increase the generalizability of the study results to the population of R/R MCL patients treated with lenalidomide.

12 OTHER INFORMATION

None.

13 CONCLUSION

This final study report provides insight into the occurrence of TFR and early deaths in patients with R/R MCL treated with lenalidomide in a real-world clinical setting. During the study period, the incidence of TFR was 5.9% and the incidence of early death was 19.8%. In addition, despite the small MCL patient population, the results of this study suggest that patients with higher tumour burden at baseline have a higher risk of TFR compared with those whose tumour burden is lower at baseline. Thus, treating physicians may consider more closely monitoring those patients with higher tumour burden after initiating lenalidomide treatment, as recommended in the currently approved SmPC. Finally, no new safety concerns were identified in this study, which is aligned with the results of the previous trials; therefore, there are no changes required regarding safety concerns as reflected in the current RMP and SmPC.

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15 ANNEX 1. LIST OF STAND-ALONE DOCUMENTS

Number	Document Reference	Number Title
1	Appendix 1.1	Protocol and Protocol Amendments
2	Appendix 1.2	Sample Case Report Form
3	Appendix 1.3	Informed Consent Forms
4	Appendix 1.4	List of Investigators
5	Appendix 1.5	Documentation of Statistical Methods
6	Appendix 1.6	Statistical Tables
7	Appendix 1.7	Listings

16 ANNEX 2. ADDITIONAL INFORMATION

NA

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APPENDIX 1.1 Protocol and Protocol Amendments

131 page(s) excluding cover page

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APPENDIX 1.1 Protocol and Protocol Amendments

- Protocol Amendment 2 - Version 5.0 Dated 20 May 2022
- Protocol Amendment 1 - Version 4.0 Dated 16 September 2019
- Initial Protocol - Version 3.0 Dated 27 March 2017

TITLE PAGE

Title	A Non-interventional, Post-authorization Safety Study of Patients with Relapsed or Refractory Mantle Cell Lymphoma to Further Investigate and Characterize the Association of Lenalidomide With Tumor Flare Reaction and High Tumor Burden
Protocol version identifier	CC-5013-MCL-005 (Version 5.0), also known as CA078-P33
Report date	20-May-2022
Date of last version of protocol	16-Sep-2019 (Version 4.0)
EU PAS register number	EUPAS23366
Active substance	Lenalidomide (ATC code: L04AX04)
Medicinal product	Revlimid®
Product reference	EU/1/07/391/001-014
Procedure number	EMEA/H/C/000717/II/79
Marketing authorization holder (MAH)	Bristol-Myers Squibb Pharma EEIG
Joint PASS	No
Research question and objectives	This study is designed as a retrospective non-interventional study of patients with relapsed or refractory (R/R) mantle cell lymphoma (MCL) to further investigate the following objectives: Primary Objective To quantify and characterize the event of tumor flare reaction (TFR) by tumor burden (assessed based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting. Secondary Objective To quantify and characterize the proportion of early deaths (defined as deaths within 20 weeks of the initial administration of lenalidomide) by tumor burden in R/R MCL patients treated with lenalidomide in a real-world setting.
Countries of study	The study will be performed in Europe. Potential sites will be identified where R/R MCL patients have been treated with lenalidomide and where lenalidomide is reimbursed for this indication. Identification of sites will be done through partnerships such as, but not limited to that with the European Mantle Cell Lymphoma Registry. Other sources including knowledge of, or experience with sites can also be used for site identification purposes. Identified sites will be assessed for feasibility and invited to participate in the study.

Authors	[redacted]

Marketing Authorization Holder(s)

Marketing authorization holder	[redacted]
MAH contact person	[redacted]

CONFIDENTIAL

This protocol is provided to you as an Investigator, potential Investigator, or consultant for review by you, your staff, and ethics committee/institutional review board. The information contained in this document is regarded as confidential and, except to the extent necessary to obtain informed consent, may not be disclosed to another party unless such disclosure is required by law or regulations. Persons to whom the information is disclosed must be informed that the information is confidential and may not be further disclosed by them.

SIGNATURE PAGE

{See appended electronic signature page}

Signature of Celgene Therapeutic Area Head

[redacted]

Printed Name of Celgene Therapeutic Area Head

Date Signed _____

{See appended electronic signature page}

Signature of Celgene Qualified Person for Pharmacovigilance

[redacted]

Printed Name of Qualified Person for Pharmacovigilance

Date Signed _____

SIGNATURE PAGE

[redacted]

Signature of Celgene Therapeutic Area Head

[redacted]

Printed Name of Celgene Therapeutic Area Head

Date Signed 10 June 2022

[redacted]

Signature of Celgene Qualified Person for Pharmacovigilance

[redacted]

Printed Name of Qualified Person for Pharmacovigilance

Date Signed 10 June 2022

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1 LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse event
CHMP	Committee for Medicinal Products for Human Use
CI	Confidence interval
CLL	Chronic lymphocytic leukemia
CRO	Contract research organization
CTCAE	Common Terminology Criteria for Adverse Events
EC	European Commission
ECOG PS	Eastern Cooperative Oncology Group Performance Status
eCRF	Electronic case report form
EDC	Electronic data capture
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EU	European Union
GVP	Good Pharmacovigilance Practices
HR	Hazard ratio
ICF	Informed consent form
IMiD®	IMiDs are a proprietary series of drugs with immunomodulatory and other properties
IQR	Interquartile range
MAH	Marketing authorization holder
MCL	Mantle cell lymphoma
MDS	Myelodysplastic syndrome
MM	Multiple myeloma
NHL	Non-Hodgkin's lymphoma
NIS	Non-interventional study
PAS	Post-authorization study
PASS	Post-authorization safety study
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan
R/R	Relapsed or refractory
SAE	Serious adverse event
SAP	Statistical analysis plan
SmPC	Summary of Product Characteristics
TEAE	Treatment-emergent adverse event

Abbreviation	Definition
TFR	Tumor flare reaction
UN	United Nation
US	United States

SUMMARY OF KEY CHANGES PROTOCOL AMENDMENT 5-0

Significant changes included in this amendment are summarized below:

- **Marketing Authorization Holder**

The marketing authorization holder (MAH) for Revlimid® has been changed to Bristol-Myers Squibb Pharma EEIG and the protocol has been updated to reflect this change. The MAH contact person has been updated.

Revised: Title Page.

- **Abstract**

The main reason for this protocol amendment was to adjust the study size based on challenges with recruitment. Despite efforts to increase recruitment, the proposed sample size will not be feasible in the proposed time period for the study. Additional factors limiting participation in this study include enrollment of patients only where lenalidomide is reimbursed, the introduction of new agents for R/R MCL, and a significant number of clinical trials for investigational agents in R/R MCL. Due to these challenges, a practical and feasible recruitment period and study size are proposed.

Revised: Section 3 Abstract

- **Summary of Protocol Amendments**

Table 2 has been updated to summarize main changes implemented through this Amendment Version 5.

Revised: Section 4 Amendments and Updates.

- **Milestones**

The milestones have been updated to reflect the estimated end of data collection and the final report of study results.

Revised: Abstract; Section 5 Milestones.

- **Common Terminology Criteria for Adverse Events (CTCAE) Version**

Clarification of the Common Terminology Criteria for Adverse Events (CTCAE) version was included to provide a common definitional framework for the AEs collected as part of this study

Revised: Section 10 Management and Reporting of Adverse Events/ Adverse Reactions

- **Key Personnel**

Key personnel have been updated to reflect changes in the responsible staff at the time of finalization of this amendment.

Revised: Title Page; Signature Page; Section 2 Responsible Parties.

- **Study Size**

The study size section has been updated with new calculations.

Revised: Abstract; Section 8.5 Study Size.

- **Other**

Various editorial changes have been made. Various typographical and grammatical errors have been corrected as appropriate. New references have been added.

2 RESPONSIBLE PARTIES

For inquiries regarding this post-authorization safety study (PASS) protocol in relapsed or refractory mantle cell lymphoma (R/R MCL), contact information is provided in Table 1.

Table 1: Contact Information for Operational Inquiries

Sponsor:	[redacted]
Contract Research Organization (CRO):	[redacted]
CRO Study Manager:	[redacted]
Celgene Global Trial Manager:	[redacted]
Celgene Physician:	[redacted]

CRO, contract research organization.

3 ABSTRACT

Title: A Non-interventional, Post-authorization Safety Study of Patients with Relapsed or Refractory Mantle Cell Lymphoma to Further Investigate and Characterize the Association of Lenalidomide With Tumor Flare Reaction and High Tumor Burden

Rationale and background:

In the European Union (EU), the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion on 28 Jan 2016 for the use of lenalidomide in the treatment of adult patients with relapsed or refractory mantle cell lymphoma. The European Commission (EC) granted a marketing authorization for this indication on 08 Jul 2016.

While the marketing authorization was granted, the Pharmacovigilance Risk Assessment Committee (PRAC) review of the Risk Management Plan (RMP) led to a request for further assessment of safety issues via post marketing surveillance. This relapsed or refractory mantle cell lymphoma (R/R MCL) post-authorization safety study (PASS) will gather additional safety information as a multinational, non-interventional study (NIS) to further investigate the primary and secondary objectives described below.

Research question and objectives:

This study is designed as a retrospective non-interventional study of patients with R/R MCL to further investigate the following objectives:

Primary Objective

To quantify and characterize the event of tumor flare reaction (TFR) by tumor burden (assessed based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting.

Secondary Objective

To quantify and characterize the proportion of early deaths (defined as deaths within 20 weeks of the initial administration of lenalidomide) by tumor burden in R/R MCL patients treated with lenalidomide in a real-world setting.

Study design:

This is a European multinational, retrospective, non-interventional study of patients with R/R MCL.

Potential sites will be identified where R/R MCL patients have been treated with lenalidomide. Site inclusion will be limited to countries where lenalidomide is reimbursed for this indication. Identification of sites will be done through partnerships such as, but not limited to that with the European Mantle Cell Lymphoma Registry. Other sources including knowledge of, or experience with sites can also be used for site identification purposes. Identified sites will then be assessed for feasibility and invited to participate in the study.

All data will be collected retrospectively from identified patients following the first dose of lenalidomide treatment for up to 6 months including those patients who died within this data collection period.

A common set of key variables in accordance with the study objectives will be identified in the medical records of eligible MCL patients and will be entered into an electronic case report form (eCRF).

Population:

The study population will consist of a retrospective cohort of R/R MCL patients who have commenced treatment with lenalidomide after 08 Jul 2016 (date EC marketing authorization was granted).

Inclusion Criteria:

- Received at least one dose of lenalidomide commencing after 08 Jul 2016 for the treatment of R/R MCL.
- Informed consent of the patient or an authorized third person or authority, if required by law, given prior to data collection.
- Patient must be ≥18 years of age.

Exclusion Criteria:

- Patients will be excluded if they were participating in an interventional clinical trial during the treatment period under observation in this PASS.

Recruitment will continue until all selected sites have been activated and all potential patients from those sites have been enrolled by Q4 2023. The target study size based on actual and projected enrolment is 100 R/R MCL patients exposed to lenalidomide.

Variables:

Variables to be evaluated in this study include baseline demographic and clinical variables (the *"population dataset"*), treatment variables related to lenalidomide use and other relevant medications (the *"treatment dataset"*), and the outcome variables for safety (the *"outcomes dataset"*).

Data sources:

Data from individual patient medical charts will be used as source data. The treating physician or an authorized delegate will enter the data from these charts into the web-based eCRF. Data entry for each enrolled patient will only start at least 6 months after the first dose of lenalidomide.

Study size:

Although the exact number of R/R MCL patients treated with lenalidomide in the European Union (EU) is not known, internal data estimates the number of patients annually who receive second-line therapy in the EU5 region (France, Germany, Italy, Spain and the United Kingdom) as 1,632; and of those, 6% receive lenalidomide alone or in combination with rituximab (Decision Resources Group internal data). Additionally, an estimated 783 patients annually receive ≥ third-line therapy, of which 11% are treated with lenalidomide alone or in combination with rituximab. The numbers of patients receiving lenalidomide for additional lines of therapy after third-line would be expected to be very low. Based on these internal estimates, approximately 184 cases per year of R/R MCL patients potentially receive second- or third-line lenalidomide treatment. However, these estimates for treatment with lenalidomide are higher than published real-world data on treatment patterns for R/R MCL (2.3% to 2.7% usage of lenalidomide in second-line treatment).[1,2,3] Further limitations on the feasibility of recruiting patients include enrolling patients only where lenalidomide is reimbursed, the introduction of new agents for R/R MCL, and a significant number of clinical trials for investigational agents in R/R MCL.

Therefore, based on the above and given that there are no additional patients retrospectively treated with lenalidomide at the active sites, recruitment of a fixed number of 100 patients is considered feasible within the estimated study selection period.

Estimation of the cumulative incidence of TFR

The calculation of precision for the cumulative incidence of TFR is based upon the observed cumulative incidence of TFR (9.6%) in the CC-5013-MCL-002 study of 167 R/R MCL patients treated with lenalidomide with an exact two-sided 95% CI = (5.6%; 15.1%). From the CC-5013-MCL-002 study, there is a 20% chance that the cumulative incidence of TFR would exceed 12.0% (upper limit of the one-sided 80% CI).

Under the assumption of a true TFR cumulative incidence rate of 9.6%, the precision on the estimate of the TFR cumulative incidence rate with 100 patients is 7.5% (upper limit of the exact two-sided 95% CI).

Under the assumption of a true TFR cumulative incidence rate of 12% in the study population, the precision on the estimate of the TFR cumulative incidence rate with 100 patients is 8.0% (upper limit of the exact two-sided 95% CI).

Estimation of early death rate

In Study CC-5013-MCL-002, 13.2% (22/167) of lenalidomide-treated patients died early. The exact two-sided 95% CI was (8.4%; 19.3%), and there is only a 20% chance that the early death rate would exceed 15.9% (upper limit of the one-sided 80% CI).

With 100 patients, the study will allow a calculation of the early death rate with a precision of +8.2% for the upper limit of the exact two-sided 95% CI if the observed rate is 13.2%, and +8.7% if it is 15.9%.

Data analysis:

The analysis will be descriptive and no *a priori* hypotheses will be tested. A statistical analysis plan (SAP) will be developed for this study. All analyses will be stratified according to baseline tumor burden.

Demographic and baseline clinical characteristics will be tabulated. Dose and duration of lenalidomide and other relevant concomitant medications will be described. The proportion of patients with high tumor burden at baseline will be estimated with its two-sided 95% CI. In this study, high tumor burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.

Tumor flare reaction is an adverse event that presents with painful lymph nodes and/or painful spleen enlargement, and can be accompanied by fever, rash, or lymphocytosis. Early death is defined as any death occurring within 20 weeks of the initial administration of lenalidomide. The cumulative incidence rate of TFR at 6 months and the proportion of early deaths (both with their exact two-sided 95% CIs) will be calculated.

The frequency of TFR and other adverse events related to lenalidomide collected and not listed in the current EU Summary of Product Characteristics (SmPC) will also be reported in summary tables. Because TFR occurs early in the course of treatment, any TFR events will be descriptively reported for up to 6 months of treatment. Tumor flare reaction will be characterized by clinical assessments and laboratory tests, and tabulated by frequency, severity, seriousness, time to onset, treatment outcome (treatment discontinuation, dose interruption or dose reduction), time to resolution, and relationship to lenalidomide and tumor burden.

In time to event analyses, cumulative incidence rates for TFR and death will be estimated using the Kaplan-Meier (KM) method. Since data is being collected retrospectively, the number of time points each patient may have will be unknown *a priori*. Given that the precision of the KM method varies with the number of time points available for analysis and that TFR is likely to occur early in treatment with lenalidomide (time to TFR is less than 5 days for almost 25% of patients experiencing TFR and the interquartile range for time to TFR in Study MCL-002 was [0.7, 2.4] weeks),[4] there will likely be an impact on the precision of the estimate using this method.

As a consequence, KM analyses will not be performed as primary but as complementary analyses.

For KM analyses, the censoring rules applying to patients for whom the event was not observed during the 6-month period following the first lenalidomide dose will be the following:

- Any patient for whom information may exist in the source database after the 6-month period following the first lenalidomide dose will be censored at 6 months.
- Any patient for whom no information exists in the source database after the 6-month period following the first lenalidomide dose will be censored at the date of the last information available in the 6-month period.

Exploration of factors associated with TFR and with early death will be conducted in multivariate analyses.

Milestones:

- Start of data collection: Q1 2019
- Estimated end of data collection: Q4 2023
- Study progress reports:
  - With annual Periodic Safety Update Reports (PSURs)
- Registration in the EU post-authorization study (PAS) register: 03 May 2018
- Final report of study results: Q4 2024

4 AMENDMENTS AND UPDATES

Table 2: Amendments and Updates

Number /Date	Main Changes
Amendment1 (Version 4.0)	The purpose of this amendment was to make practical changes to the study data sources regarding the cohorts and site inclusion processes. There is now only one data source with standardized site selection, patient identification, and data management practices. Furthermore, additional clarification has been provided to ensure that data entry will start only 6 months after the first lenalidomide dose and regarding inclusion of patients who have died and cannot consent. Practical details such as key study personnel and MAH holder have also been updated. The statistical section has been modified to further specify analyses to be performed and to define baseline variables. Creatinine clearance has been included as a variable for analysis.
Amendment 2 (Version 5.0)	The purpose of this amendment was to revise the study size and study milestones based on challenges with recruitment. Therefore, the Study Size section and Study Milestones were updated to reflect this change. Practical details, such as key study personnel, have also been updated. Clarification of the Common Terminology Criteria for Adverse Events versions has also been included.

5 MILESTONES

Milestones for this study are summarized in Table 3.

Table 3: Study Milestones

Milestone	Planned Date
Start of Data Collection	Q1 2019
Estimated End of Data Collection	Q4 2023
Study Progress Reports	
PSUR	Annual as per PSUR cycle
Registration in the EU PAS Registry	03 May 2018
Final Report of Study Results	Q4 2024

Q1, first quarter; Q4, fourth quarter.

6 RATIONALE AND BACKGROUND

6.1 Rationale

Lenalidomide is a member of a proprietary series of drugs with immunomodulatory and other properties, referred to as IMiDs®[1].

In the United States (US), lenalidomide received regulatory approval on 05 Jun 2013, for the treatment of patients with mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib. In the European Union (EU), the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion on 28-Jan-2016 for the use of lenalidomide in the treatment of adult patients with relapsed or refractory mantle cell lymphoma. The European Commission (EC) granted a marketing authorization for this indication on 08 Jul 2016.

While the marketing authorization was granted, the Pharmacovigilance Risk Assessment Committee (PRAC), after reviewing the Risk Management Plan (RMP), requested further assessment of safety issues via post marketing surveillance. This relapsed or refractory (R/R) MCL PASS will aim to gather additional safety information as a multinational, non-interventional study (NIS) to further investigate the research objectives described in Section 7.2.

6.2 Background

Mantle cell lymphoma is a type of non-Hodgkin's lymphoma (NHL), currently defined as per the World Health Organization Classification of Tumours of Haemaotopoietic and Lymphoid Tissues[5] with differing clinical features and responses to treatment.[6] The annual incidence of MCL in Europe was estimated as 0.45 cases per 100,000 persons based on cancer registry data from 20 countries.[7] Patients with MCL typically are predominantly male and Caucasian with a median age of > 60 years, and present with advanced stage disease. Despite intensive induction therapies in the front-line setting of young and fit patients, the clinical course is typically that of repeated relapses, and median survival of MCL is only 3 to 5 years.[8,9]

6.2.1 Study CC-5013-MCL-002

Study CC-5013-MCL-002 (SPRINT; hereinafter Study MCL-002), ClinicalTrials.gov number: NCT00875667, was the main study and basis for the marketing authorization for the R/R MCL indication granted on 08 Jul 2016 by the EC.

Study MCL-002 was a randomized, Phase 2 study of patients with MCL aged 18 years or older at 67 clinics and academic centers in 12 countries who relapsed 1 to 2 times, had Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 to 2, at least 1 measurable lesion to be eligible, and who were ineligible for intensive chemotherapy or stem-cell transplantation.

Between 30 Apr 2009 and 07 Mar 2013, 254 patients were enrolled: 170 (67%) were randomly assigned to receive lenalidomide (Lenalidomide Arm), 84 (33%) to receive investigator's choice monotherapy (Control Arm). Patients had a median age of 68.5 years and received a median of 2 previous regimens. With a median follow-up of 15.9 months, lenalidomide significantly

[1] IMiDs® are a proprietary series of drugs with immunomodulatory and other properties.

improved progression-free survival compared with investigator's choice (median 8.7 months [95% confidence interval {CI}: 5.5, 12.1] versus 5.2 months [95% CI: 3.7, 6.9]) with a hazard ratio (HR) of 0.61 (95% CI: 0.44, 0.84; p = 0·004). In the 167 patients in the Lenalidomide Arm and 83 patients in the Control Arm who received at least one dose of treatment, the most common Grade 3 or 4 adverse events (AEs), respectively, included neutropenia (73 [44%] versus 28 [34%]) without increased risk of infection; thrombocytopenia (30 [18%] versus 23 [28%]); leucopenia (13 [8%] vs 9 [11%]); and anemia (14 [8%] vs 6 [7%]).[4]

6.2.2 Tumor Flare Reaction in Study MCL-002

Tumor flare reaction (TFR) is an AE that is associated with treatment of patients with lymphoma or chronic lymphocytic leukemia (CLL) with immunomodulatory drugs due to their specific mode of action, but not with chemotherapy.[10,11,12,13,14,15,16,17,18,19] It clinically presents with painful lymph nodes and/or spleen enlargement and can be accompanied by fever, rash, or lymphocytosis. Tumor flare reaction has been reported as a new important identified risk specific to lenalidomide treatment of CLL and B-cell lymphomas, but was not reported in association with the other target populations for Revlimid® (multiple myeloma [MM]; myelodysplastic syndrome [MDS]). Tumor flare reaction usually develops early in the course of therapy and may mimic progression of disease and subsides and resolves over time. Symptomatic treatment is used depending on the severity of the TFR.

In Study MCL-002, TFR was reported in the Lenalidomide Arm only (16 of 167 patients, [9.6%]) but not in the Control Arm (single-agent therapy with chemotherapy or rituximab). Of these 16 TFR events, the events in 3 (1.8%) subjects were classified as Grade 3 or 4 events (no Grade 5 AEs were reported): 1 event (0.6%) was a serious AE (SAE) (Celgene data on file) and 1 event (0.6%) resulted in treatment discontinuation. All TFR events occurred in Cycle 1 of treatment, except for 1 TFR event that started in Cycle 2. The median time to TFR was 1.1 weeks (interquartile range [IQR]: 0.7, 2.4).[4]

The variables that remained in the final multivariate model in Study MCL-002, which were strongly and independently correlated with TFR included high Mantle Cell Lymphoma International Prognostic Index (MIPI) score at diagnosis (p = 0.084) and bulky disease at baseline (p = 0.020).

In Study MCL-002, no SAEs of TFR were observed in the group of subjects with high absolute lymphocyte count (> 15 g/L) at baseline. Therefore, these subjects do not seem to be at a particularly high risk for such events, supporting the analyses for TFR in which an elevated site blood cell count at baseline was not an independent risk factor for the occurrence of TFR.

In the Revlimid Summary of Product Characteristics (SmPC), TFR has been listed as an adverse drug reaction (Revlimid SmPC Section 4.8),[20] added as a specific warning (Revlimid SmPC Section 4.4),[20] and cited as an important identified risk in the RMP (Version 37.0).

6.2.3 Tumor Burden and Early Deaths in Study MCL-002

In Study MCL-002, there was an overall risk reduction of 11% for the secondary endpoint overall survival (OS) when comparing the Lenalidomide Arm to the Control Arm (HR of 0.89 [95% CI,

0.62, 1.28]; p = 0.519, log-rank test). However, there was also an increase in deaths within 20 weeks from randomization (early deaths) in lenalidomide-treated patients (22/167 [13.2%]) in the Lenalidomide Arm versus 6/83 (7.2%) patients treated in the Control Arm.

It is important to note that there was an imbalance in important baseline disease-related risk factors between treatment arms, which disfavored subjects in the Lenalidomide Arm. This included high-risk MIPI scores, elevated levels of lactate dehydrogenase, bulky disease, and high tumor burden, all of which were more frequently observed in the Lenalidomide Arm. The proportion of patients with high tumor burden (defined by at least one lesion 5 cm or more in diameter or three lesions 3 cm or more in diameter by central radiology review) in the Lenalidomide Arm was 81 (48%) of 170 patients versus 28 (33%) of 84 patients in the Control Arm (investigator's choice of monotherapy with either chlorambucil, cytarabine, rituximab, fludarabine, or gemcitabine).[4]

Additional analyses were done to further characterize these early deaths with respect to disease-related characteristics. Based on a multivariate analysis, only high tumor burden at baseline was identified as a significant risk factor for early death. Treatment was not identified as a risk factor in the multivariate analysis.

The proportion of subjects with high tumor burden at baseline who died within 20 weeks (19.8% versus 7.1%) and within 52 weeks (39.5% versus 21.4%) after randomization was greater in the Lenalidomide Arm compared with the Control Arm (Celgene data on file).

In the Lenalidomide Arm, 11 (13.6%) of the 81 subjects who had high tumor burden at baseline discontinued treatment during Cycle 1 and the majority of these (7 of 11 subjects) did so due to treatment-emergent adverse events (TEAEs). In comparison, 4 (5.1%) of the 78 subjects who had low tumor burden at baseline discontinued treatment during Cycle 1; the majority of these (3 of 4 subjects) also discontinued treatment due to TEAEs (Celgene data on file).

In the Control Arm, 1 (3.6%) of the 28 subjects who had high tumor burden at baseline discontinued treatment during Cycle 1 (Celgene data on file).

Based on the above data, high tumor burden is a relevant factor for early death, regardless of treatment arm. However, it remains possible that the presence of TFR, an adverse event related to lenalidomide use, could have contributed to the early death in addition to high tumor burden. This hypothesis could not be tested given that there is no TFR case in the control group. It is unfortunate that in the MCL-002 study,[4] the protocol did not use tumor burden at baseline as a stratification factor.

7 RESEARCH QUESTION AND OBJECTIVES

7.1 Research Question

This study is designed as a retrospective non-interventional study of patients with R/R MCL to further investigate the research objectives described in Section 7.2.

7.2 Research Objectives

7.2.1 Primary Objective

To quantify and characterize the event of TFR by tumor burden (assessed based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting.

7.2.2 Secondary Objective(s)

To quantify and characterize the proportion of early deaths (defined as deaths within 20 weeks of initial administration of lenalidomide) by tumor burden in R/R MCL patients treated with lenalidomide in a real-world setting.

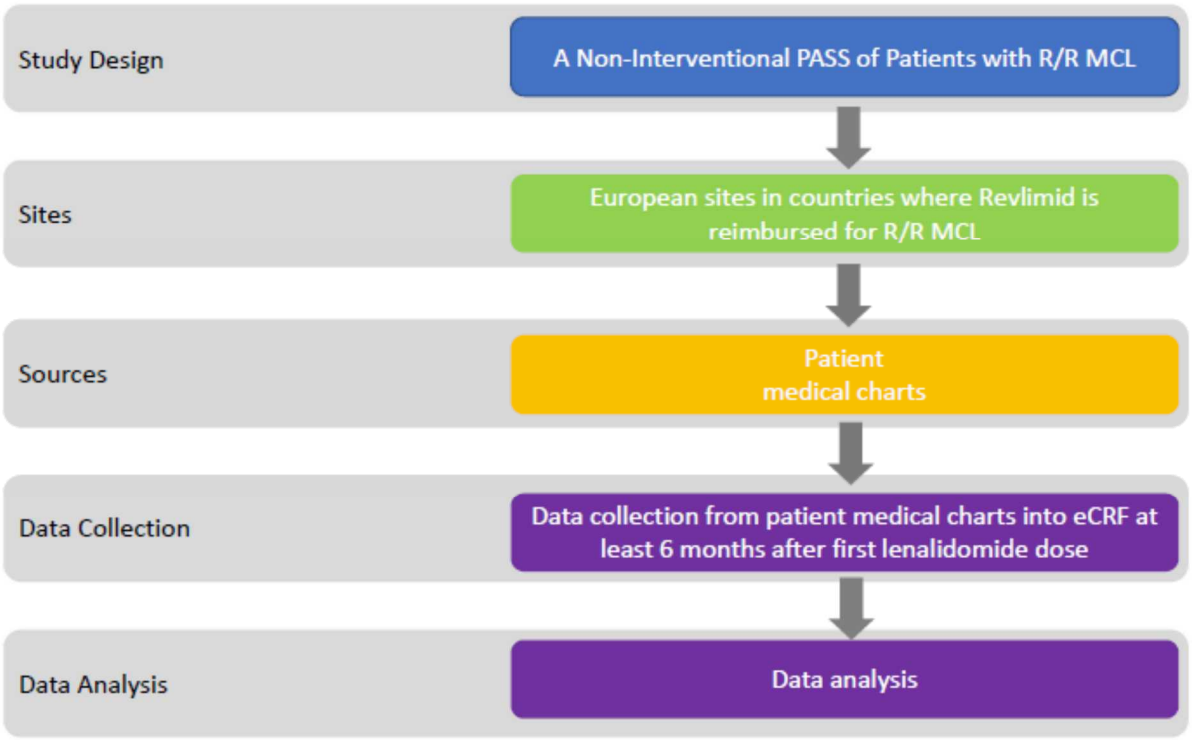
8 RESEARCH METHODS

8.1 Study Design and Selection Criteria

8.1.1 Study Design

This is a European multinational, retrospective, non-interventional study of patients with R/R MCL. Figure 1 provides a high-level schematic of the design of the study.

Figure 1: Study Design



eCRF, electronic case report form; PASS; post-authorization safety study.

The study will be performed in Europe. Potential sites will be identified where R/R MCL patients have been treated with lenalidomide and where lenalidomide is reimbursed for this indication. Identification of sites will be done through partnerships such as, but not limited to that with the European Mantle Cell Lymphoma Registry. Other sources including knowledge of, or experience with sites can also be used for site identification purposes. Identified sites will be assessed for feasibility and invited to participate in the study.

All data will be collected retrospectively from identified patients following the first dose of lenalidomide treatment for up to 6 months including those patients who died within this data collection period.

More details about the identification of sites and patients are provided in Section 8.4 (Data Sources).

8.1.2 Selection Criteria

8.1.2.1 Inclusion Criteria

1) Received at least one dose of lenalidomide commencing after 08 Jul 2016 for the treatment of R/R MCL.
2) Informed consent of the patient or an authorized third person or authority, if required by law, given prior to data collection.
3) Patient must be ≥18 years of age.

8.1.2.2 Exclusion Criteria

1) Patients will be excluded if they were participating in an interventional clinical trial during the treatment period under observation in this PASS.

8.2 Setting

Study Population

The study population will consist of a retrospective cohort of R/R MCL patients who have commenced treatment with lenalidomide after 08 Jul 2016 (date marketing authorization was granted). Three datasets will be described for the study population and will form the basis of subsequent analyses:

Population dataset

Treatment dataset

Outcomes dataset

8.3 Variables

Variables to be evaluated in this study include baseline demographic and clinical variables (*"population dataset"*) (Table 4), treatment variables related to lenalidomide use and other relevant medications (*"treatment dataset"*) (Table 5), and the outcome variables for safety (*"outcomes dataset"*) (Table 6).

Table 4: Demographics and Clinical Variables

Variables	Data to be Collected
Demographics	
Age	Age (years)
Sex	Female/male
Clinical Variables	
Informed consent	Date of consent

Table 4: Demographics and Clinical Variables

Variables	Data to be Collected
MCL	Date of initial MCL diagnosis; MIPI score at initial diagnosis; Bulky Disease at initial diagnosis; Prior stem cell transplantation (autologous/allogeneic); Date of last relapse/disease progression before lenalidomide therapy; Time from last dose of last therapy before lenalidomide therapy
Medical history	Prior history of TFR; Cardiovascular events (eg, arrhythmia and coronary artery disease); Cerebrovascular events (eg, TIA and stroke); Thromboembolic events (arterial and venous [eg, DVT, PE, and MI]); Peripheral/autonomic neuropathy; Pulmonary, hepatic, renal disease; History of other malignant diseases; Other relevant concomitant diseases or medical conditions
Disease-related characteristics	Tumor burden (high tumor burden is defined as at least one lesion of ≥ 5 cm diameter or at least 3 lesions of ≥3 cm diameter); Bulky disease (≥7 cm) at beginning of lenalidomide treatment; ECOG PS
Relevant Concomitant Medications related to TFR treatment and/or prophylaxis	Description of Concomitant Medication Indication of Concomitant Medication Start date of Concomitant Medication
Laboratory tests	Hematology: hemoglobin, platelets, WBC, ANC, ALC Biochemistry: LDH, creatinine, creatinine clearance, blood glucose, bilirubin, albumin, ALT, AST, calcium, phosphorus, sodium, potassium, CRP

ALC, absolute lymphocyte count; ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; CRP, C-reactive protein; DVT, deep vein thrombosis; LDH, lactic dehydrogenase; MI, myocardial infarction; PE, pulmonary embolism; TIA, transient ischemic attack; WBC, white blood cell.

Table 5: Lenalidomide Therapy and Other Treatment Variables

Variables	Data to be Collected
Previous treatments	Number of previous lines of treatment; Description of previous treatments
Lenalidomide treatment	(Date of start and end of treatment [dd/mm/yyyy], lenalidomide dose and regimen, reason for lenalidomide discontinuation or any interruption of therapy with lenalidomide, dose adjustments, where applicable)

Table 6: Outcome Variables for Safety

Variables	Data to be Collected
TFR (physician reported)	Adverse Event reported in eCRF/Medical file (onset date, stop date, severity, seriousness, clinical signs and symptoms, lab tests, treatment outcome [treatment discontinuation, dose interruption or dose reduction], relationship to lenalidomide)
TFR symptoms and signs	Painful lymph nodes, painful spleen enlargement, fever[a], rash[a], lymphocytosis[a].
Other AEs	Adverse events related to lenalidomide and not listed in current EU SmPC
Death	Date and cause

[a] Fever, rash, or lymphocytosis alone do not constitute TFR.

A study flowchart provides additional details on the data that will be collected before and during lenalidomide treatment (Table 7).

Table 7: Study Flow Chart Showing Collection of Data Before and During Course of Lenalidomide Treatment

	Pretreatment	During Treatment
Informed Consent[a]		
Demographic Data	X	
Medical History	X	
MIPI Score	X	
Prior Stem Cell Transplantation	X	
ECOG PS	X	
Relevant Concomitant Medication	X	X
Tumor Burden Assessment	X[b]	
TFR symptoms and signs	X	X
Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC		X
Available identified laboratory data[c]	X	X

[a] Patient informed consent, or agreement with a competent authority or another authorized third party (eg, next of kin), is to be obtained prior to data collection.

[b] Tumor burden assessment based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide.

[c] See laboratory tests in Table 4.

8.4 Data Sources

Data from individual patient medical charts will be used as source data. The treating physician or an authorized delegate will enter the data from these medical charts into the web-based eCRF (secondary use of data). A common set of key variables (see Section 8.3) will be collected. Data entry for each enrolled patient will only start at least 6 months after the first dose of lenalidomide.

8.5 Study Size

Although the exact number of R/R MCL patients treated with lenalidomide in the European Union (EU) is not known, internal data estimates the number of patients annually who receive second-line therapy in the EU5 region (France, Germany, Italy, Spain and the United Kingdom) as 1,632; and of those, 6% receive lenalidomide alone or in combination with rituximab (Decision Resources Group internal data). Additionally, an estimated 783 patients annually receive ≥ third-line therapy, of which 11% are treated with lenalidomide alone or in combination with rituximab. The numbers of patients receiving lenalidomide for additional lines of therapy after third-line would be expected to be very low. Based on these internal estimates, approximately 184 cases per year of R/R MCL patients potentially receive second- or third-line lenalidomide treatment. However, these estimates for treatment with lenalidomide are higher than published real-world data on treatment patterns for R/R MCL (2.3% to 2.7% usage of lenalidomide in second-line treatment).[1,2,3] Further limitations on the feasibility of recruiting patients include enrolling patients only where lenalidomide is reimbursed, the introduction of new agents for R/R MCL, and a significant number of clinical trials for investigational agents in R/R MCL.

Therefore, based on the above and given that there are no additional patients retrospectively treated with lenalidomide at the active sites, recruitment of a fixed number of 100 patients is considered feasible within the estimated study selection period.

Estimation of the cumulative incidence of TFR

The calculation of precision for the cumulative incidence of TFR is based upon the observed cumulative incidence of TFR (9.6%) in the CC-5013-MCL-002 study of 167 R/R MCL patients treated with lenalidomide with an exact two-sided 95% CI = (5.6%; 15.1%). From the CC-5013-MCL-002 study, there is a 20% chance that the cumulative incidence of TFR would exceed 12.0% (upper limit of the one-sided 80% CI).

Under the assumption of a true TFR cumulative incidence rate of 9.6%, the precision on the estimate of the TFR cumulative incidence rate with 100 patients is 7.5% (upper limit of the exact two-sided 95% CI).

Under the assumption of a true TFR cumulative incidence rate of 12% in the study population, the precision on the estimate of the TFR cumulative incidence rate with 100 patients is 8.0% (upper limit of the exact two-sided 95% CI).

Estimation of early death rate

In Study CC-5013-MCL-002, 13.2% (22/167) of lenalidomide-treated patients died early. The exact two-sided 95% CI was (8.4%; 19.3%), and there is only a 20% chance that the early death rate would exceed 15.9% (upper limit of the one-sided 80% CI).

With 100 patients, the study will allow a calculation of the early death rate with a precision of +8.2% for the upper limit of the exact two-sided 95% CI if the observed rate is 13.2%, and +8.7% if it is 15.9%.

8.6 Data Management

Data for the MCL PASS will be collected once patient records are complete, ie, if 6 months have elapsed after a patient received the first lenalidomide dose.

The data will be collected using an eCRF. For each patient, data will be collected in compliance with the applicable local legislation.

The data collected via an eCRF will be electronically verified through use of programmed edit checks. Discrepancies in the data will be brought to the attention of the team, and investigational site personnel, if necessary. Resolution of these issues will be reflected in the database. An audit trail within the system will track all changes made to the data.

Celgene will ensure that appropriate quality review procedures are performed during and after data collection. Accuracy will be checked through programmatic edit checks according to the standard quality control procedures at the institutions conducting the data collection. The CRO will issue queries to the site for resolution. Any necessary corrections will be then applied to the data in the eCRF. If necessary, source data verification (ie, a direct comparison of the entries made in the eCRF against the patient's notes) may be conducted in a selected subgroup of sites.

8.7 Data Analysis

The analysis will be descriptive and no *a priori* hypotheses will be tested. A statistical analysis plan (SAP) will be developed for this study. All analyses will be stratified according to baseline tumor burden. A baseline variable is defined as the latest pre-treatment measure or information within a variable-specific window as specified in the SAP.

Demographic and baseline clinical characteristics will be tabulated. Dose and duration of lenalidomide and other relevant concomitant medications will be described. The proportion of patients with high tumor burden at baseline will be estimated with its two-sided 95% CI. In this study, high tumor burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.

Tumor flare reaction is an AE that presents with painful lymph nodes and/or painful spleen enlargement, and can be accompanied by fever, rash, or lymphocytosis. Early death is defined as any death occurring within 20 weeks of the initial administration of lenalidomide. The cumulative incidence rate of TFR and the proportion of early deaths (both with their exact two-sided 95% CIs) will be calculated.

The frequency of TFR and other adverse events related to lenalidomide collected and not listed in the current EU Summary of Product Characteristics (SmPC) will also be reported in summary tables. Because TFR occurs early in the course of treatment, any TFR events will be descriptively reported for up to 6 months of treatment. Tumor flare reaction will be characterized by clinical assessments and laboratory tests, and tabulated by frequency, severity, seriousness, time to onset, treatment outcome (treatment discontinuation, dose interruption or dose reduction), time to resolution, and relationship to lenalidomide and tumor burden.

In time to event analyses, cumulative incidence rates for TFR and death will be estimated using the Kaplan-Meier (KM) method. Since data is being collected retrospectively, the number of time

points each patient may have will be unknown *a priori*. Given that the precision of the KM method varies with the number of time points available for analysis and that TFR is likely to occur early in treatment with lenalidomide (time to TFR is less than 5 days for almost 25% of patients experiencing TFR and the interquartile range for time to TFR in Study MCL-002 was [0.7, 2.4] weeks),[4] there will likely be an impact on the precision of the estimate using this method.

As a consequence, KM analyses will not be performed as primary but as complementary analyses.

For KM analyses, the censoring rules applying to patients for whom the event was not observed during the 6-month period following the first lenalidomide dose will be the following:

- Any patient for whom information may exist in the source database after the 6-month period following the first lenalidomide dose will be censored at 6 months.
- Any patient for whom no information exists in the source database after the 6-month period following the first lenalidomide dose will be censored at the date of the last information available in the 6-month period.

Exploration of factors associated with TFR and with early death will be conducted in multivariate analyses.

8.8 Quality Control

All data collected for the MCL PASS should be recorded accurately.

Security of the data will be maintained at all times in line with applicable local law and procedures. Access will be limited to authorized individuals. Controls, such as document encryption, will be used to ensure the authenticity, integrity, and confidentiality of electronic records when transmitted over open systems (eg, the internet). Adequate back up of the data will be maintained throughout the course of the study.

The following activities aim to ensure data quality by checking the accuracy of the data collected from medical charts, checking the completeness and validity of data in the electronic data capture (EDC) through:

- Monitoring:
  - Performing source data verification (samples rather than 100%) to ensure EDC data match source data
- Data Management:
  - Using edit checks mainly within the EDC system for more efficient data cleaning and for identification of critical missing data, required data fields, illogical, and inconsistent data

8.9 Limitations of the Research Methods

All AEs (as documented in the medical charts) collected in the study that are related to lenalidomide but not listed in the current EU SmPC will be summarized and frequencies calculated. Since the study is designed with TFR as the main outcome, it may not be sufficiently powered to provide a precise estimate for these adverse reactions. However, events captured

through the review of medical records will be an improvement on spontaneous reporting as these events may not have been captured through normal channels.

Although a multivariate model will be attempted to explore the relationship between TFR and early death, the sample size may not be sufficiently powered and interpretation of results should be limited to hypothesis generation. There are also limitations to the Kaplan-Meier analysis as the retrospective nature of the study and the secondary use of the data may not allow for all the information needed with appropriate time precision and correspondence with the expected time to these events.

8.10 Other Aspects

Not applicable.

9 PROTECTION OF HUMAN SUBJECTS

Data will be collected from patients who have given their informed consent or, in case it's not applicable, data will be collected in accordance with local legislation. For patients who have died and therefore cannot provide consent, local requirements will be followed.

This study will complete all regulatory and ethical review requirements in accordance with applicable regulations.

Given that this is a non-interventional study, it does not give rise to additional risks for the safety of the patients.

10 MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

This R/R MCL study is based upon secondary use of data. Reporting requirements for this non-interventional study are described in Module VI of the European Medicines Agency (EMA) Guideline on Good Pharmacovigilance Practices (GVP). Module VI (EMA, 2016)[21] provides that "For non-interventional study designs which are based on secondary use of data, adverse reactions reporting is not required. Reports of adverse events/reactions should only be summarized in the study report, where applicable."

In addition to the information relevant to the primary objective, information on AEs related to lenalidomide and not listed in the current EU SmPC (Revlimid SmPC Section 4.8)[20] will be collected. Common Terminology Criteria for Adverse Events (CTCAE) will be used to identify the incidence, but not the severity of the identified AEs as the study is based on retrospective data collection. The CTCAE will be used where feasible to provide a common definitional framework for the AEs collected as part of this study. CTCAE Version 3.0 will be used to grade TFR, and all other AEs will be graded using CTCAE Version 5.0.

As required by the GVP modules for Periodic Safety Update Reports (PSURs) (Module VII [EMA, 2013])[22] and RMPs (Module V [EMA, 2016]),[23] information on collected AEs related to lenalidomide will be included in the study report and reported appropriately in both the PSUR and the RMP. In cases of doubt, the reporting requirements will be clarified with the authorities concerned of the EU Member States.

11 PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

Regular safety updates will be made as per regulatory requirements via the PSURs. Interim analysis communications may be pursued if medical need arises.

Final data will be appropriately communicated when available, through presentation at major European or global congresses of hematology and/or oncology. Final results of the R/R MCL PASS also will be submitted for publication to an appropriate scientific and medical journal. Authorship will be based on scientific contribution to the study design and on enrollment of evaluable patients.

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[23] European Medicines Agency (EMA). Guideline on Good Pharmacovigilance Practices (GVP). Module V – Risk management systems (Rev 2). Draft for public consultation, 24 Feb 2016, EMA/838713/2011.

ANNEX 1. LIST OF STAND-ALONE DOCUMENTS

None.

ANNEX 2. ENCEPP CHECKLIST FOR STUDY PROTOCOLS

Doc.Ref. EMA/540136/2009

• ENCePP Checklist for Study Protocols (Revision 4)

Adopted by the ENCePP Steering Group on 15/10/2018

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) welcomes innovative designs and new methods of research. This Checklist has been developed by ENCePP to stimulate consideration of important principles when designing and writing a pharmacoepidemiological or pharmacovigilance study protocol. The Checklist is intended to promote the quality of such studies, not their uniformity. The user is also referred to the ENCePP Guide on Methodological Standards in Pharmacoepidemiology, which reviews and gives direct electronic access to guidance for research in pharmacoepidemiology and pharmacovigilance.

For each question of the Checklist, the investigator should indicate whether or not it has been addressed in the study protocol. If the answer is "Yes", the section number of the protocol where this issue has been discussed should be specified. It is possible that some questions do not apply to a particular study (for example, in the case of an innovative study design). In this case, the answer 'N/A' (Not Applicable) can be checked and the "Comments" field included for each section should be used to explain why. The "Comments" field can also be used to elaborate on a "No" answer.

This Checklist should be included as an Annex by marketing authorisation holders when submitting the protocol of a non-interventional post-authorisation safety study (PASS) to a regulatory authority (see the Guidance on the format and content of the protocol of non-interventional post-authorisation safety studies). The Checklist is a supporting document and does not replace the format of the protocol for PASS presented in the Guidance and Module VIII of the Good pharmacovigilance practices (GVP).

Study title:

EU PAS Register® number: **Study reference number (if applicable):**

Section 1: Milestones	**Yes**	**No**	**N/A**	**Section Number**
1.1 Does the protocol specify timelines for				5
1.1.1 Start of data collection[2]	☒	☐	☐	
1.1.2 End of data collection[3]	☒	☐	☐	
1.1.3 Progress report(s)	☒	☐	☐	
1.1.4 Interim report(s)	☐	☒	☐	

[2] Date from which information on the first study is first recorded in the study dataset or, in the case of secondary use of data, the date from which data extraction starts.
[3] Date from which the analytical dataset is completely available.

Section 1: Milestones	**Yes**	**No**	**N/A**	**Section Number**
1.1.5 Registration in the EU PAS Register®	☒	☐	☐	
1.1.6 Final report of study results.	☒	☐	☐	

Comments:

Section 2: Research question	**Yes**	**No**	**N/A**	**Section Number**
2.1 Does the formulation of the research question and objectives clearly explain:	☒	☐	☐	6,7,8
2.1.1 Why the study is conducted? (e.g. to address an important public health concern, a risk identified in the risk management plan, an emerging safety issue)	☒	☐	☐	
2.1.2 The objective(s) of the study?	☒	☐	☐	
2.1.3 The target population? (i.e. population or subgroup to whom the study results are intended to be generalised)	☒	☐	☐	
2.1.4 Which hypothesis(-es) is (are) to be tested?	☐	☒	☐	
2.1.5 If applicable, that there is no *a priori* hypothesis?	☐	☐	☒	

Comments:

These is no hypothesis testing therefore there is no a prior hypothesis

Section 3: Study design	**Yes**	**No**	**N/A**	**Section Number**
3.1 Is the study design described? (e.g. cohort, case-control, cross-sectional, other design)	☒	☐	☐	8.1
3.2 Does the protocol specify whether the study is based on primary, secondary or combined data collection?	☒	☐	☐	8.1, 8.4
3.3 Does the protocol specify measures of occurrence? (e.g., rate, risk, prevalence)	☒	☐	☐	8.7
3.4 Does the protocol specify measure(s) of association? (e.g. risk, odds ratio, excess risk, rate ratio, hazard ratio, risk/rate difference, number needed to harm (NNH))	☐	☒	☐	

Section 3: Study design	**Yes**	**No**	**N/A**	**Section Number**
3.5 Does the protocol describe the approach for the collection and reporting of adverse events/adverse reactions? (e.g. adverse events that will not be collected in case of primary data collection)	☒	☐	☐	10

Comments:

Section 4: Source and study populations	**Yes**	**No**	**N/A**	**Section Number**
4.1 Is the source population described?	☒	☐	☐	8.2
4.2 Is the planned study population defined in terms of:				8.1-8.2
4.2.1 Study time period	☒	☐	☐	
4.2.2 Age and sex	☐	☒	☐	
4.2.3 Country of origin	☐	☒	☐	
4.2.4 Disease/indication	☒	☐	☐	
4.2.5 Duration of follow-up	☒	☐	☐	
4.3 Does the protocol define how the study population will be sampled from the source population? (e.g. event or inclusion/exclusion criteria)	☒	☐	☐	8.1

Comments:

Section 5: Exposure definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
5.1 Does the protocol describe how the study exposure is defined and measured? (e.g. operational details for defining and categorising exposure, measurement of dose and duration of drug exposure)	☒	☐	☐	8.1-8.3
5.2 Does the protocol address the validity of the exposure measurement? (e.g. precision, accuracy, use of validation sub-study)	☐	☒	☐	
5.3 Is exposure categorised according to time windows?	☐	☒	☐	
5.4 Is intensity of exposure addressed? (e.g. dose, duration)	☐	☒	☐	

Section 5: Exposure definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
5.5 Is exposure categorised based on biological mechanism of action and taking into account the pharmacokinetics and pharmacodynamics of the drug?	☐	☒	☐	
5.6 Is (are) (an) appropriate comparator(s) identified?	☐	☐	☒	

Comments:

The aim of the study is to quantify the outcomes of interest and not a comparative study

Section 6: Outcome definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
6.1 Does the protocol specify the primary and secondary (if applicable) outcome(s) to be investigated?	☒	☐	☐	7
6.2 Does the protocol describe how the outcomes are defined and measured?	☒	☐	☐	8.1-8.3
6.3 Does the protocol address the validity of outcome measurement? (e.g. precision, accuracy, sensitivity, specificity, positive predictive value, use of validation sub-study)	☐	☒	☐	
6.4 Does the protocol describe specific outcomes relevant for Health Technology Assessment? (e.g. HRQoL, QALYs, DALYS, health care services utilisation, burden of disease or treatment, compliance, disease management)	☐	☒	☐	

Comments:

Section 7: Bias	**Yes**	**No**	**N/A**	**Section Number**
7.1 Does the protocol address ways to measure confounding? (e.g. confounding by indication)	☐	☒	☐	
7.2 Does the protocol address selection bias? (e.g. healthy user/adherer bias)	☐	☐	☒	
7.3 Does the protocol address information bias? (e.g. misclassification of exposure and outcomes, time-related bias)	☐	☐	☒	

Comments:

This study is designed to measure the rate of events in outcomes of interest in patients exposure to lenalidomide therefore selection bias and information bias are not applicable here.

Section 8: Effect measure modification	**Yes**	**No**	**N/A**	**Section Number**
8.1 Does the protocol address effect modifiers? (e.g. collection of data on known effect modifiers, sub-group analyses, anticipated direction of effect)	☐	☐	☒	

Comments:

This is not a comparative study therefore no measures of effect will be estimated and effect modifiers are not relevant.

Section 9: Data sources	**Yes**	**No**	**N/A**	**Section Number**
9.1 Does the protocol describe the data source(s) used in the study for the ascertainment of:				
9.1.1 Exposure? (e.g. pharmacy dispensing, general practice prescribing, claims data, self-report, face-to-face interview)	☒	☐	☐	8.4
9.1.2 Outcomes? (e.g. clinical records, laboratory markers or values, claims data, self-report, patient interview including scales and questionnaires, vital statistics)	☒	☐	☐	8.4
9.1.3 Covariates and other characteristics?	☒	☐	☐	8.4
9.2 Does the protocol describe the information available from the data source(s) on:				
9.2.1 Exposure? (e.g. date of dispensing, drug quantity, dose, number of days of supply prescription, daily dosage, prescriber)	☐	☒	☐	
9.2.2 Outcomes? (e.g. date of occurrence, multiple event, severity measures related to event)	☐	☒	☐	
9.2.3 Covariates and other characteristics? (e.g. age, sex, clinical and drug use history, co-morbidity, co-medications, lifestyle)	☐	☒	☐	
9.3 Is a coding system described for:				
9.3.1 Exposure? (e.g. WHO Drug Dictionary, Anatomical Therapeutic Chemical (ATC) Classification System)	☐	☒	☐	
9.3.2 Outcomes? (e.g. International Classification of Diseases (ICD), Medical Dictionary for Regulatory Activities (MedDRA))	☐	☒	☐	
9.3.3 Covariates and other characteristics?	☐	☒	☐	
9.4 Is a linkage method between data sources described? (e.g. based on a unique identifier or other)	☐	☒	☐	

Comments:

Section 10: Analysis plan	**Yes**	**No**	**N/A**	**Section Number**
10.1 Are the statistical methods and the reason for their choice described?	☒	☐	☐	8.7
10.2 Is study size and/or statistical precision estimated?	☒	☐	☐	8.5
10.3 Are descriptive analyses included?	☒	☐	☐	8.7
10.4 Are stratified analyses included?	☐	☐	☒	
10.5 Does the plan describe methods for analytic control of confounding?	☐	☐	☒	
10.6 Does the plan describe methods for analytic control of outcome misclassification?	☐	☐	☒	
10.7 Does the plan describe methods for handling missing data?	☐	☐	☒	
10.8 Are relevant sensitivity analyses described?	☐	☒	☐	

Comments:

Given the goal of the study is to estimate the rate of outcome event and not a comparative study, items 10.4-10.7 does not apply.

Section 11: Data management and quality control	**Yes**	**No**	**N/A**	**Section Number**
11.1 Does the protocol provide information on data storage? (e.g. software and IT environment, database maintenance and anti-fraud protection, archiving)	☒	☐	☐	8.6
11.2 Are methods of quality assurance described?	☒	☐	☐	8.6
11.3 Is there a system in place for independent review of study results?	☐	☒	☐	

Comments:

Section 12: Limitations	**Yes**	**No**	**N/A**	**Section Number**
12.1 Does the protocol discuss the impact on the study results of:				
12.1.1 Selection bias?	☐	☒	☐	
12.1.2 Information bias?	☐	☐	☒	

Section 12: Limitations	**Yes**	**No**	**N/A**	**Section Number**
12.1.3 Residual/unmeasured confounding? (e.g. anticipated direction and magnitude of such biases, validation sub-study, use of validation and external data, analytical methods).	☐	☐	☒	
12.2 Does the protocol discuss study feasibility? (e.g. study size, anticipated exposure uptake, duration of follow-up in a cohort study, patient recruitment, precision of the estimates)	☒	☐	☐	8.9

Comments:

As the study is descriptive and no comparisons are conducted, information bias and confounding are not relevant.

Section 13: Ethical/data protection issues	**Yes**	**No**	**N/A**	**Section Number**
13.1 Have requirements of Ethics Committee/ Institutional Review Board been described?	☐	☒	☐	
13.2 Has any outcome of an ethical review procedure been addressed?	☒	☐	☐	9
13.3 Have data protection requirements been described?	☒	☐	☐	9

Comments:

Section 14: Amendments and deviations	**Yes**	**No**	**N/A**	**Section Number**
14.1 Does the protocol include a section to document amendments and deviations?	☒	☐	☐	4

Comments:

Section 15: Plans for communication of study results	**Yes**	**No**	**N/A**	**Section Number**
15.1 Are plans described for communicating study results (e.g. to regulatory authorities)?	☒	☐	☐	11
15.2 Are plans described for disseminating study results externally, including publication?	☒	☐	☐	11

Comments:

Name of the main authors of the protocol: [redacted]

Date: 01-Jun-2022

Signature: [redacted]

Date: 01-Jun-2022

Signature: [redacted]

ANNEX 3. ADDITIONAL INFORMATION

Not applicable.

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Title	A Non-interventional, Post-authorization Safety Study of Patients with Relapsed or Refractory Mantle Cell Lymphoma to Further Investigate and Characterize the Association of Lenalidomide With Tumor Flare Reaction and High Tumor Burden
Protocol version identifier	CC-5013-MCL-005 (Version 4.0)
Date of last version of protocol	07 Aug 2017 (Version 3.0)
EU PAS register number	EUPAS23366
Active substance	Lenalidomide (ATC code: L04AX04)
Medicinal product	Revlimid®
Product reference	EU/1/07/391/001-009
Procedure number	EMEA/H/C/000717/II/79
Marketing authorization holder	Celgene Europe B.V.
Joint PASS	No
Research question and objectives	This study is designed as a retrospective non-interventional study of patients with relapsed or refractory (R/R) mantle cell lymphoma (MCL) to further investigate the following objectives: Primary Objective To quantify and characterize the event of tumor flare reaction (TFR) by tumor burden (assessed based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting. Secondary Objective To quantify and characterize the proportion of early deaths (defined as deaths within 20 weeks of the initial administration of lenalidomide) by tumor burden in R/R MCL patients treated with lenalidomide in a real-world setting.
Countries of study	The study will be performed in Europe. Potential sites will be identified where R/R MCL patients have been treated with lenalidomide and where lenalidomide is reimbursed for this indication. Identification of sites will be done through partnerships such as, but not limited to that with the European Mantle Cell Lymphoma Registry. Other sources including knowledge of, or experience with sites can also be used for site identification purposes. Identified sites will be assessed for feasibility and invited to participate in the study.

Authors	[redacted]

Marketing Authorization Holder(s)

Marketing authorization holder	[redacted]
MAH contact person	[redacted]

CONFIDENTIAL

This protocol is provided to you as an Investigator, potential Investigator, or consultant for review by you, your staff, and ethics committee/institutional review board. The information contained in this document is regarded as confidential and, except to the extent necessary to obtain informed consent, may not be disclosed to another party unless such disclosure is required by law or regulations. Persons to whom the information is disclosed must be informed that the information is confidential and may not be further disclosed by them.

SIGNATURE PAGE

{See appended electronic signature page}

_____

Signature of Celgene Therapeutic Area Head

[redacted]

Printed Name of Celgene Therapeutic Area Head

Date Signed _____

{See appended electronic signature page}

_____

Signature of Celgene Qualified Person for Pharmacovigilance

[redacted]

Printed Name of Qualified Person for Pharmacovigilance

Date Signed _____

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2. LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse event
CHMP	Committee for Medicinal Products for Human Use
CI	Confidence interval
CLL	Chronic lymphocytic leukemia
CRO	Contract research organization
CTCAE	Common Terminology Criteria for Adverse Events
EC	European Commission
ECOG PS	Eastern Cooperative Oncology Group Performance Status
eCRF	Electronic case report form
EDC	Electronic data capture
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EU	European Union
GVP	Good Pharmacovigilance Practices
HR	Hazard ratio
ICF	Informed consent form
IMiD®	IMiDs are a proprietary series of drugs with immunomodulatory and other properties
IQR	Interquartile range
MAH	Marketing authorization holder
MCL	Mantle cell lymphoma
MDS	Myelodysplastic syndrome
MM	Multiple myeloma
NDMCL	Newly diagnosed mantle cell lymphoma
NHL	Non-Hodgkin's lymphoma
NIS	Non-interventional study
PAS	Post-authorization study
PASS	Post-authorization safety study
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan
R/R	Relapsed or refractory
SAE	Serious adverse event

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Abbreviation	Definition
SAP	Statistical analysis plan
SmPC	Summary of Product Characteristics
TEAE	Treatment-emergent adverse event
TFR	Tumor flare reaction
UN	United Nation
US	United States

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3. RESPONSIBLE PARTIES

For inquiries regarding this post-authorization safety study (PASS) protocol in relapsed or refractory mantle cell lymphoma (R/R MCL), contact information is provided in Table 1.

Table 1: Contact Information for Operational Inquiries

Sponsor:	[redacted]
Contract Research Organization (CRO):	[redacted]
CRO Study Manager:	[redacted]
Celgene Study Manager:	[redacted]
Celgene Physician:	[redacted]

CRO = contract research organization.

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4. ABSTRACT

Title: A Non-interventional, Post-authorization Safety Study of Patients with Relapsed or Refractory Mantle Cell Lymphoma to Further Investigate and Characterize the Association of Lenalidomide With Tumor Flare Reaction and High Tumor Burden

Rationale and background:

In the European Union (EU), the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion on 28 Jan 2016 for the use of lenalidomide in the treatment of adult patients with relapsed or refractory mantle cell lymphoma. The European Commission (EC) granted a marketing authorization for this indication on 08 Jul 2016.

While the marketing authorization was granted, the Pharmacovigilance Risk Assessment Committee (PRAC) review of the Risk Management Plan (RMP) led to a request for further assessment of safety issues via post marketing surveillance. This relapsed or refractory mantle cell lymphoma (R/R MCL) post-authorization safety study (PASS) will gather additional safety information as a multinational, non-interventional study (NIS) to further investigate the primary and secondary objectives described below.

Research question and objectives:

This study is designed as a retrospective non-interventional study of patients with R/R MCL to further investigate the following objectives:

Primary Objective

To quantify and characterize the event of tumor flare reaction (TFR) by tumor burden (assessed based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting.

Secondary Objective

To quantify and characterize the proportion of early deaths (defined as deaths within 20 weeks of the initial administration of lenalidomide) by tumor burden in R/R MCL patients treated with lenalidomide in a real-world setting.

Study design:

This is a European multinational, retrospective, non-interventional study of patients with R/R MCL.

Potential sites will be identified where R/R MCL patients have been treated with lenalidomide. Site inclusion will be limited to countries where lenalidomide is reimbursed for this indication. Identification of sites will be done through partnerships such as, but not limited to that with the European Mantle Cell Lymphoma Registry. Other sources including knowledge of, or experience with sites can also be used for site identification purposes. Identified sites will then be assessed for feasibility and invited to participate in the study.

All data will be collected retrospectively from identified patients following the first dose of lenalidomide treatment for up to 6 months including those patients who died within this data collection period.

A common set of key variables in accordance with the study objectives will be identified in the medical records of eligible MCL patients and will be entered into an electronic case report from (eCRF).

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Population:

The study population will consist of a retrospective cohort of R/R MCL patients who have commenced treatment with lenalidomide after 08 Jul 2016 (date EC marketing authorization was granted).

Inclusion Criteria:

1) Received at least one dose of lenalidomide commencing after 08 Jul 2016 for the treatment of R/R MCL.
2) Informed consent of the patient or an authorized third person or authority, if required by law, given prior to data collection.
3) Patient must be ≥18 years of age.

Exclusion Criteria:

1) Patients will be excluded if they were participating in an interventional clinical trial during the treatment period under observation in this PASS.

Recruitment will continue until at least 560 R/R MCL patients exposed to lenalidomide are included in the study.

Variables:

Variables to be evaluated in this study include baseline demographic and clinical variables (the *"population dataset"*), treatment variables related to lenalidomide use and other relevant medications (the *"treatment dataset"*), and the outcome variables for safety (the *"outcomes dataset"*).

Data sources:

Data from individual patient medical charts will be used as source data. The treating physician or an authorized delegate will enter the data from these charts into the web-based eCRF. Data entry for each enrolled patient will only start at least 6 months after the first dose of lenalidomide.

Study size:

The incidence of newly diagnosed MCL (NDMCL) is 0.45 cases per 100,000 per year (Sant, 2010). With a population of 738,442,000 in Europe in 2015 (United Nations [UN] estimate), the number of NDMCL cases per year is estimated at 3,323. Of these, 67% are expected to be relapsed or refractory resulting in 2,226 R/R MCL cases per year (3,323 x 0.67).

Assuming a 10% use of lenalidomide as second-line treatment in these patients by 2018 results in an estimated 223 cases per year (2,226 x 0.10). Assuming that 60% of R/R MCL patients receive second-line treatment and that 25% of these receive third-line lenalidomide treatment by 2018 leads to an estimated 334 cases (2,226 x 0.6 x 0.25). This then gives an estimated 557 (223 + 334) cases per year of R/R MCL patients receiving second- or third-line lenalidomide treatment.

Sample size required for estimation of the cumulative incidence of TFR

Sample size calculation is based upon the observed cumulative incidence of TFR (9.6%) in the CC-5013-MCL-002 study of 167 R/R MCL patients treated with lenalidomide with an exact two-sided 95% CI = (5.6%; 15.1%). From the CC-5013-MCL-002 study, there is a 20% chance that the cumulative incidence of TFR would exceed 12.0% (upper limit of the one-sided 80% CI).

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Under the assumption of a true TFR cumulative incidence rate of 9.6%, 497 patients are needed for reaching a precision of +3% on the estimate of the TFR cumulative incidence rate (upper limit of the exact two-sided 95% CI).

A sample size of 558 is required should the observed incidence of TFR reach 12% in the study population. This would give a precision of +3% based on the upper limit of the exact two-sided 95% CI. Therefore, a sample size of 560 patients will be targeted.

Estimation of early death rate

In Study CC-5013-MCL-002, 13.2% (22/167) of lenalidomide-treated patients died early. The exact two-sided 95% CI was (8.4%; 19.3%), and there is only a 20% chance that the early death rate would exceed 15.9% (upper limit of the one-sided 80% CI).

With 560 patients, the study will allow a calculation of the early death rate with a precision of +3.1% for the upper limit of the exact two-sided 95% CI if the observed rate is 13.2%, and +3.4% if it is 15.9%.

Based on market projections for lenalidomide in R/R MCL patients in Europe, the proposed study will need to accrue patients for 8 years.

Data analysis:

The analysis will be descriptive and no *a priori* hypotheses will be tested. A statistical analysis plan (SAP) will be developed for this study. All analyses will be stratified according to baseline tumor burden.

Demographic and baseline clinical characteristics will be tabulated. Dose and duration of lenalidomide and other relevant concomitant medications will be described. The proportion of patients with high tumor burden at baseline will be estimated with its two-sided 95% CI. In this study, high tumor burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.

Tumor flare reaction is an AE that presents with painful lymph nodes and/or painful spleen enlargement, and can be accompanied by fever, rash, or lymphocytosis. Early death is defined as any death occurring within 20 weeks of the initial administration of lenalidomide. The cumulative incidence rate of TFR at 6 months and the proportion of early deaths (both with their exact two-sided 95% CIs) will be calculated.

The frequency of TFR and other adverse events related to lenalidomide collected and not listed in the current EU Summary of Product Characteristics (SmPC) will also be reported in summary tables. Because TFR occurs early in the course of treatment, any TFR events will be descriptively reported for up to 6 months of treatment. Tumor flare reaction will be characterized by clinical assessments and laboratory tests, and tabulated by frequency, severity, seriousness, time to onset, treatment outcome (treatment discontinuation, dose interruption or dose reduction), time to resolution, and relationship to lenalidomide and tumor burden.

In time to event analyses, cumulative incidence rates for TFR and death will be estimated using the Kaplan-Meier (KM) method. Since data is being collected retrospectively, the number of time points each patient may have will be unknown *a priori*. Given that the precision of the KM method varies with the number of time points available for analysis and that TFR is likely to occur early in treatment with lenalidomide (time to TFR is less than 5 days for almost 25% of patients experiencing TFR and the interquartile range for time to TFR in Study MCL-002 was [0.7, 2.4] weeks [Trněný, 2016]), there will likely be an impact on the precision of the estimate using this method.

As a consequence, KM analyses will not be performed as primary but as complementary analyses.

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For KM analyses, the censoring rules applying to patients for whom the event was not observed during the 6-month period following the first lenalidomide dose will be the following:

• Any patient for whom information may exist in the source database after the 6-month period following the first lenalidomide dose will be censored at 6 months.

• Any patient for whom no information exists in the source database after the 6-month period following the first lenalidomide dose will be censored at the date of the last information available in the 6-month period.

Exploration of factors associated with TFR and with early death will be conducted in multivariate analyses.

Milestones:

- Start of data collection: Q1 2019
- Estimated end of data collection: Q4 2026
- Study progress reports:
  - With annual Periodic Safety Update Reports (PSURs)
- Registration in the EU post-authorization study (PAS) register: 03 May 2018
- Final report of study results: Q4 2027

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5. AMENDMENTS AND UPDATES

Table 2: Amendments and Updates

Number /Date	Main Changes
Amendment1 (Version 4.0)	The purpose of this amendment was to make practical changes to the study data sources regarding the cohorts and site inclusion processes. There is now only one data source with standardized site selection, patient identification, and data management practices. Furthermore, additional clarification has been provided to ensure that data entry will start only 6 months after the last lenalidomide dose and regarding inclusion of patients who have died and cannot consent. Practical details such as key study personnel and MAH holder have also been updated. The statistical section has been modified to further specify analyses to be performed and to define baseline variables. Creatinine clearance has been included as a variable for analysis.

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6. MILESTONES

Milestones for this study are summarized in Table 3.

Table 3: Study Milestones

Milestone	Planned Date
Start of Data Collection	Q1 2019
Estimated End of Data Collection	Q4 2026
Study Progress Reports	
PSUR	Annual as per PSUR cycle
Registration in the EU PAS Registry	03 May 2018
Final Report of Study Results	Q4 2027

EU = European Union; PAS = post-authorization study; PSUR = Periodic Safety Update Report; Q1 = first quarter; Q4 = fourth quarter.

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7. RATIONALE AND BACKGROUND

7.1. Rationale

Lenalidomide is a member of a proprietary series of drugs with immunomodulatory and other properties, referred to as IMiDs®[1].

In the United States (US), lenalidomide received regulatory approval on 05 Jun 2013, for the treatment of patients with mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib. In the European Union (EU), the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion on 28 Jan 2016 for the use of lenalidomide in the treatment of adult patients with relapsed or refractory mantle cell lymphoma. The European Commission (EC) granted a marketing authorization for this indication on 08 Jul 2016.

While the marketing authorization was granted, the Pharmacovigilance Risk Assessment Committee (PRAC), after reviewing the Risk Management Plan (RMP), requested further assessment of safety issues via post marketing surveillance. This relapsed or refractory (R/R) MCL PASS will aim to gather additional safety information as a multinational, non-interventional study (NIS) to further investigate the research objectives described in Section 8.2.

7.2. Background

Mantle cell lymphoma is a type of non-Hodgkin's lymphoma (NHL), currently defined as per the World Health Organization Classification of Tumours of Haemaotopoietic and Lymphoid Tissues (Swerdlow, 2016) with differing clinical features and responses to treatment (Armitage, 1993). The annual incidence of MCL in Europe was estimated as 0.45 cases per 100,000 persons based on cancer registry data from 20 countries (Sant, 2010). Patients with MCL typically are predominantly male and Caucasian with a median age of > 60 years, and present with advanced stage disease. Despite intensive induction therapies in the front-line setting of young and fit patients, the clinical course is typically that of repeated relapses, and median survival of MCL is only 3 to 5 years (Abrahamsson, 2014; Salek, 2014).

7.2.1. Study CC-5013-MCL-002

Study CC-5013-MCL-002 (SPRINT; hereinafter Study MCL-002), ClinicalTrials.gov number: NCT00875667, was the main study and basis for the marketing authorization for the R/R MCL indication granted on 08 Jul 2016 by the EC.

Study MCL-002 was a randomized, Phase 2 study of patients with MCL aged 18 years or older at 67 clinics and academic centers in 12 countries who relapsed 1 to 2 times, had Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 to 2, at least 1 measurable lesion to be eligible, and who were ineligible for intensive chemotherapy or stem-cell transplantation.

[1] IMiDs® are a proprietary series of drugs with immunomodulatory and other properties.

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Between 30 Apr 2009 and 07 Mar 2013, 254 patients were enrolled: 170 (67%) were randomly assigned to receive lenalidomide (Lenalidomide Arm), 84 (33%) to receive investigator's choice monotherapy (Control Arm). Patients had a median age of 68.5 years and received a median of 2 previous regimens. With a median follow-up of 15.9 months, lenalidomide significantly improved progression-free survival compared with investigator's choice (median 8.7 months [95% confidence interval {CI}: 5.5, 12.1] versus 5.2 months [95% CI: 3.7, 6.9]) with a hazard ratio (HR) of 0.61 (95% CI: 0.44, 0.84; p = 0·004). In the 167 patients in the Lenalidomide Arm and 83 patients in the Control Arm who received at least one dose of treatment, the most common Grade 3 or 4 adverse events (AEs), respectively, included neutropenia (73 [44%] versus 28 [34%]) without increased risk of infection; thrombocytopenia (30 [18%] versus 23 [28%]); leucopenia (13 [8%] vs 9 [11%]); and anemia (14 [8%] vs 6 [7%]) (Trněný, 2016).

7.2.2. Tumor Flare Reaction in Study MCL-002

Tumor flare reaction is an AE that is associated with treatment of patients with lymphoma or chronic lymphocytic leukemia (CLL) with immunomodulatory drugs due to their specific mode of action, but not with chemotherapy (Andritsos, 2008; Chanan-Khan, 2006; Chanan-Khan, 2011a; Cheson, 2016; Corazzelli, 2010; Eve, 2010a; Ferrajoli, 2008a; Goy, 2013; Kayar, 2014; Witzig, 2011). It clinically presents with painful lymph nodes and/or spleen enlargement and can be accompanied by fever, rash, or lymphocytosis. Tumor flare reaction has been reported as a new important identified risk specific to lenalidomide treatment of CLL and B-cell lymphomas, but was not reported in association with the other target populations for Revlimid® (multiple myeloma [MM]; myelodysplastic syndrome [MDS]). Tumor flare reaction usually develops early in the course of therapy and may mimic progression of disease and subsides and resolves over time. Symptomatic treatment is used depending on the severity of the TFR.

In Study MCL-002, TFR was reported in the Lenalidomide Arm only (16 of 167 patients, [9.6%]) but not in the Control Arm (single-agent therapy with chemotherapy or rituximab). Of these 16 TFR events, the events in 3 (1.8%) subjects were classified as Grade 3 or 4 events (no Grade 5 AEs were reported): 1 event (0.6%) was a serious AE (SAE) (Celgene data on file) and 1 event (0.6%) resulted in treatment discontinuation. All TFR events occurred in Cycle 1 of treatment, except for 1 TFR event that started in Cycle 2. The median time to TFR was 1.1 weeks (interquartile range [IQR]: 0.7, 2.4) (Trněný, 2016).

The variables that remained in the final multivariate model in Study MCL-002, and were strongly and independently correlated with TFR, high Mantle Cell Lymphoma International Prognostic Index (MIPI) score at diagnosis (p = 0.084) and bulky disease at baseline (p = 0.020), appeared to be risk factors for TFR.

In Study MCL-002, no SAEs of TFR were observed in the group of subjects with high absolute lymphocyte count (> 15 g/L) at baseline. Therefore, these subjects do not seem to be at a particularly high risk for such events, supporting the analyses for TFR in which an elevated site blood cell count at baseline was not an independent risk factor for the occurrence of TFR.

In the Revlimid Summary of Product Characteristics (SmPC), TFR has been listed as an adverse drug reaction (Revlimid SmPC Section 4.8), added as a specific warning (Revlimid SmPC Section 4.4), and cited as an important identified risk in the RMP (Version 34, Section 3.11).

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7.2.3. Tumor Burden and Early Deaths in Study MCL-002

In Study MCL-002, there was an overall risk reduction of 11% for the secondary endpoint overall survival (OS) when comparing the Lenalidomide Arm to the Control Arm (HR of 0.89 [95% CI, 0.62, 1.28]; p = 0.519, log-rank test). However, there was also an increase in deaths within 20 weeks from randomization (early deaths) in lenalidomide-treated patients (22/167 [13.2%]) in the Lenalidomide Arm versus 6/83 (7.2%) patients treated in the Control Arm.

It is important to note that there was an imbalance in important baseline disease-related risk factors between treatment arms, which disfavored subjects in the Lenalidomide Arm. This included high-risk MIPI scores, elevated levels of LDH, bulky disease, and high tumor burden, all of which were more frequently observed in the Lenalidomide Arm. The proportion of patients with high tumor burden (defined by at least one lesion 5 cm or more in diameter or three lesions 3 cm or more in diameter by central radiology review) in the Lenalidomide Arm was 81 (48%) of 170 patients versus 28 (33%) of 84 patients in the Control Arm (investigator's choice of monotherapy with either chlorambucil, cytarabine, rituximab, fludarabine, or gemcitabine) (Trněný, 2016).

Additional analyses were done to further characterize these early deaths with respect to disease-related characteristics. Based on a multivariate analysis, only high tumor burden at baseline was identified as a significant risk factor for early death. Treatment was not identified as a risk factor in the multivariate analysis.

The proportion of subjects with high tumor burden at baseline who died within 20 weeks (19.8% versus 7.1%) and within 52 weeks (39.5% versus 21.4%) after randomization was greater in the Lenalidomide Arm compared with the Control Arm (Celgene data on file).

In the Lenalidomide Arm, 11 (13.6%) of the 81 subjects who had high tumor burden at baseline discontinued treatment during Cycle 1 and the majority of these (7 of 11 subjects) did so due to treatment-emergent adverse events (TEAEs). In comparison, 4 (5.1%) of the 78 subjects who had low tumor burden at baseline discontinued treatment during Cycle 1; the majority of these (3 of 4 subjects) also discontinued treatment due to TEAEs (Celgene data on file).

In the Control Arm, 1 (3.6%) of the 28 subjects who had high tumor burden at baseline discontinued treatment during Cycle 1 (Celgene data on file).

Based on the above data, high tumor burden is a relevant factor for early death, regardless of treatment arm. However, it remains possible that the presence of TFR, an adverse event related to lenalidomide use, could have contributed to the early death in addition to high tumour burden. This hypothesis could not be tested given that there is no TFR case in the control group. It is unfortunate that in the MCL-002 study (Trněný, 2016), the protocol did not use tumor burden at baseline as a stratification factor.

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8. RESEARCH QUESTION AND OBJECTIVES

8.1. Research Question

This study is designed as a retrospective non-interventional study of patients with R/R MCL to further investigate the research objectives described in Section 8.2.

8.2. Research Objectives

8.2.1. Primary Objective

To quantify and characterize the event of TFR by tumor burden (assessed based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting.

8.2.2. Secondary Objective(s)

To quantify and characterize the proportion of early deaths (defined as deaths within 20 weeks of initial administration of lenalidomide) by tumor burden in R/R MCL patients treated with lenalidomide in a real-world setting.

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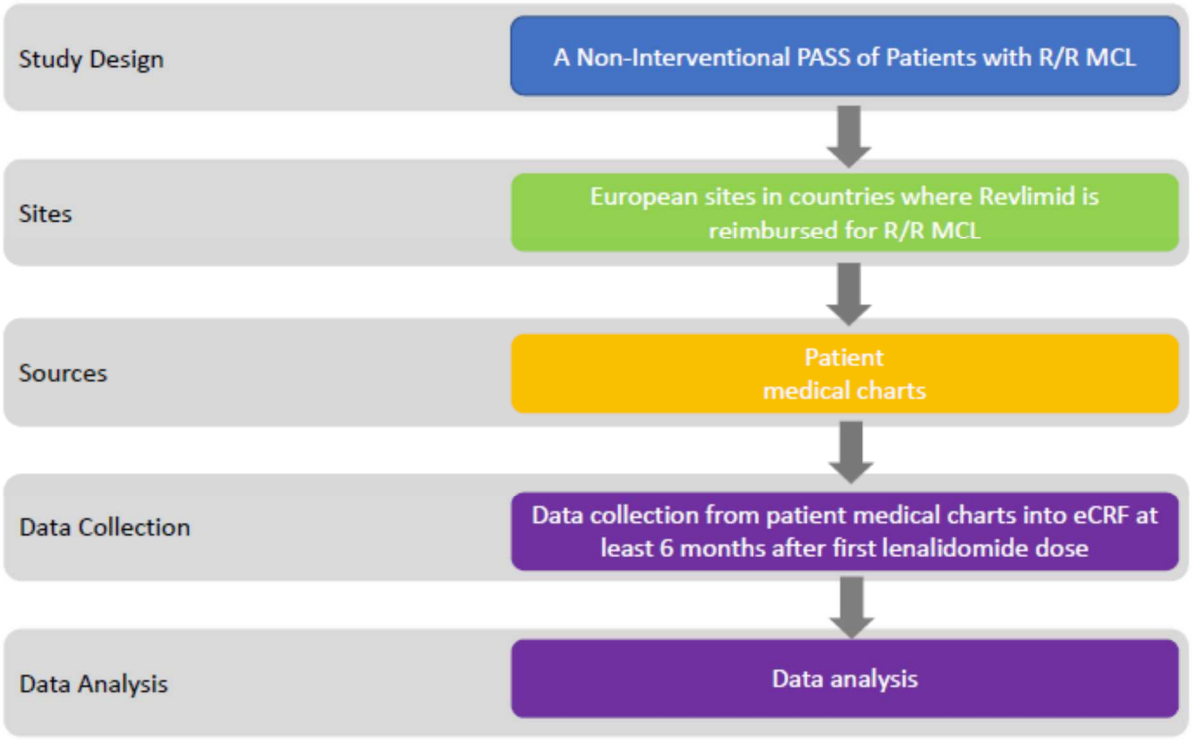
9. RESEARCH METHODS

9.1. Study Design and Selection Criteria

9.1.1. Study Design

This is a European multinational, retrospective, non-interventional study of patients with R/R MCL. Figure 1 provides a high-level schematic of the design of the study.

Figure 1: Study Design



MCL = mantle cell lymphoma; PASS = post-authorization safety study; R/R = relapsed or refractory; eCRF = electronic case report form.

The study will be performed in Europe. Potential sites will be identified where R/R MCL patients have been treated with lenalidomide and where lenalidomide is reimbursed for this indication. Identification of sites will be done through partnerships such as, but not limited to that with the European Mantle Cell Lymphoma Registry. Other sources including knowledge of, or experience with sites can also be used for site identification purposes. Identified sites will be assessed for feasibility and invited to participate in the study.

All data will be collected retrospectively from identified patients following the first dose of lenalidomide treatment for up to 6 months including those patients who died within this data collection period.

More details about the identification of sites and patients are provided in Section 9.4 (Data Sources).

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9.1.2. Selection Criteria

9.1.2.1. Inclusion Criteria

1. Received at least one dose of lenalidomide commencing after 08 Jul 2016 for the treatment of R/R MCL.
2. Informed consent of the patient or an authorized third person or authority, if required by law, given prior to data collection.
3. Patient must be ≥18 years of age.

9.1.2.2. Exclusion Criteria

1. Patients will be excluded if they were participating in an interventional clinical trial during the treatment period under observation in this PASS.

9.2. Setting

Study Population

The study population will consist of a retrospective cohort of R/R MCL patients who have commenced treatment with lenalidomide after 08 Jul 2016 (date marketing authorization was granted). Three datasets will be described for the study population and will form the basis of subsequent analyses:

- Population dataset
- Treatment dataset
- Outcomes dataset

9.3. Variables

Variables to be evaluated in this study include baseline demographic and clinical variables (*"population dataset"*) (Table 4), treatment variables related to lenalidomide use and other relevant medications (*"treatment dataset"*) (Table 5), and the outcome variables for safety (*"outcomes dataset"*) (Table 6)

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Table 4: Demographics and Clinical Variables

Variables	Data to be Collected
Demographics	
Age	Age (years)
Sex	Female/male
Clinical Variables	
Informed consent	Date of consent
MCL	Date of initial MCL diagnosis; MIPI score at initial diagnosis; Bulky Disease at initial diagnosis; Prior stem cell transplantation (autologous/allogeneic); Date of last relapse/disease progression before lenalidomide therapy; Time from last dose of last therapy before lenalidomide therapy
Medical history	Prior history of TFR; Cardiovascular events (eg, arrhythmia and coronary artery disease); Cerebrovascular events (eg, TIA and stroke); Thromboembolic events (arterial and venous [eg, DVT, PE, and MI]); Peripheral/autonomic neuropathy; Pulmonary, hepatic, renal disease; History of other malignant diseases; Other relevant concomitant diseases or medical conditions
Disease-related characteristics	Tumor burden (high tumor burden is defined as at least one lesion of ≥ 5 cm diameter or at least 3 lesions of ≥3 cm diameter); Bulky disease (≥7 cm) at beginning of lenalidomide treatment; ECOG performance status
Relevant Concomitant Medications related to TFR treatment and/or prophylaxis	Description of Concomitant Medication Indication of Concomitant Medication Start date of Concomitant Medication
Laboratory tests	Hematology: hemoglobin, platelets, WBC, ANC, ALC Biochemistry: LDH, creatinine, creatinine clearance, blood glucose, bilirubin, albumin, ALT, AST, calcium, phosphorus, sodium, potassium, CRP

ALC = absolute lymphocyte count; ALT = alanine aminotransferase; ANC = absolute neutrophil count; AST = aspartate aminotransferase; CRP = C-reactive protein; DVT = deep vein thrombosis; ECOG = Eastern Cooperative Oncology Group; LDH = lactic dehydrogenase; MCL = mantle cell lymphoma; MI = myocardial infarction; MIPI = Mantle Cell Lymphoma International Prognostic Index; PE = pulmonary embolism; TIA = transient ischemic attack; TFR = tumor flare reaction; WBC = white blood cell.

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Table 5: Lenalidomide Therapy and Other Treatment Variables

Variables	Data to be Collected
Previous treatments	Number of previous lines of treatment; Description of previous treatments
Lenalidomide treatment	(Date of start and end of treatment [dd/mm/yyyy], lenalidomide dose and regimen, reason for lenalidomide discontinuation or any interruption of therapy with lenalidomide, dose adjustments, where applicable)

Table 6: Outcome Variables for Safety

Variables	Data to be Collected
TFR (physician reported)	Adverse Event reported in eCRF/Medical file (onset date, stop date, severity, seriousness, clinical signs and symptoms, lab tests, treatment outcome [treatment discontinuation, dose interruption or dose reduction], relationship to lenalidomide)
TFR symptoms and signs	Painful lymph nodes, painful spleen enlargement, fever[a], rash[a], lymphocytosis[a].
Other AEs	Adverse events related to lenalidomide and not listed in current EU SmPC
Death	Date and cause

AE = adverse event; eCRF = electronic case report form; EU = European Union; SmPC = Summary of Product Characteristics; TFR = tumor flare reaction.
[a] Fever, rash, or lymphocytosis alone do not constitute TFR.

A study flowchart provides additional details on the data that will be collected before and during lenalidomide treatment (Table 7).

Table 7: Study Flow Chart Showing Collection of Data Before and During Course of Lenalidomide Treatment

	Pretreatment	During Treatment
Informed Consent[a]		
Demographic Data	X	
Medical History	X	
MIPI Score	X	
Prior Stem Cell Transplantation	X	
ECOG PS	X	
Relevant Concomitant Medication	X	X
Tumor Burden Assessment	X[b]	
TFR symptoms and signs	X	X
Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC		X
Available identified laboratory data[c]	X	X

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ECOG PS = Eastern Cooperative Oncology Group Performance Status; EU = European Union; MIPI = Mantle Cell Lymphoma International Prognostic Index; PS = performance status; SmPC = Summary of Product Characteristics; TFR = tumor flare reaction.

[a] Patient informed consent, or agreement with a competent authority or another authorized third party (eg, next of kin), is to be obtained prior to data collection.

[b] Tumor burden assessment based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide.

[c] See laboratory tests in Table 4

9.4. Data Sources

Data from individual patient medical charts will be used as source data. The treating physician or an authorized delegate will enter the data from these medical charts into the web-based eCRF (secondary use of data). A common set of key variables (see Section 9.3) will be collected. Data entry for each enrolled patient will only start at least 6 months after the first dose of lenalidomide.

9.5. Study Size

The incidence of newly diagnosed MCL (NDMCL) is 0.45 cases per 100,000 per year (Sant, 2010). With a population of 738,442,000 in Europe in 2015 (United Nations [UN] estimate), the number of NDMCL cases per year is estimated at 3,323. Of these, 67% are expected to be relapsed or refractory resulting in 2,226 R/R MCL cases per year (3,323 x 0.67).

Assuming a 10% use of lenalidomide as second-line treatment in these patients by 2018 results in an estimated 223 cases per year (2,226 x 0.10). Assuming that 60% of R/R MCL patients receive second-line treatment and that 25% of these receive third-line lenalidomide treatment by 2018 leads to an estimated 334 cases (2,226 x 0.6 x 0.25). This then gives an estimated 557 (223 + 334) cases per year of R/R MCL patients receiving second- or third-line lenalidomide treatment.

Sample size required for estimation of the cumulative incidence of TFR

Sample size calculation is based upon the observed cumulative incidence of TFR (9.6%) in the CC-5013-MCL-002 study of 167 R/R MCL patients treated with lenalidomide with an exact two-sided 95% CI = (5.6%; 15.1%). From the CC-5013-MCL-002 study, there is a 20% chance that the cumulative incidence of TFR would exceed 12.0% (upper limit of the one-sided 80% CI).

Under the assumption of a true TFR cumulative incidence rate of 9.6%, 497 patients are needed for reaching a precision of +3% on the estimate of the TFR cumulative incidence rate (upper limit of the exact two-sided 95% CI).

A sample size of 558 is required should the observed incidence of TFR reach 12% in the study population. This would give a precision of +3% based on the upper limit of the exact two-sided 95% CI. Therefore, a sample size of 560 patients will be targeted.

Estimation of early death rate

In Study CC-5013-MCL-002, 13.2% (22/167) of lenalidomide-treated patients died early. The exact two-sided 95% CI was (8.4%; 19.3%), and there is only a 20% chance that the early death rate would exceed 15.9% (upper limit of the one-sided 80% CI).

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With 560 patients, the study will allow a calculation of the early death rate with a precision of +3.1% for the upper limit of the exact two-sided 95% CI if the observed rate is 13.2%, and +3.4% if it is 15.9%.

Based on market projections for lenalidomide in R/R MCL patients in Europe, the proposed study will need to accrue patients for 8 years.

9.6. Data Management

Data for the MCL PASS will be collected once patient records are complete, ie, if 6 months have elapsed after a patient received the first lenalidomide dose.

The data will be collected using an eCRF. For each patient, data will be collected in compliance with the applicable local legislation.

The data collected via an eCRF will be electronically verified through use of programmed edit checks. Discrepancies in the data will be brought to the attention of the team, and investigational site personnel, if necessary. Resolution of these issues will be reflected in the database. An audit trail within the system will track all changes made to the data.

Celgene will ensure that appropriate quality review procedures are performed during and after data collection. Accuracy will be checked through programmatic edit checks according to the standard quality control procedures at the institutions conducting the data collection. The CRO will issue queries to the site for resolution. Any necessary corrections will be then applied to the data in the eCRF. If necessary, source data verification (ie, a direct comparison of the entries made in the eCRF against the patient's notes) may be conducted in a selected subgroup of sites.

9.7. Data Analysis

The analysis will be descriptive and no *a priori* hypotheses will be tested. A statistical analysis plan (SAP) will be developed for this study. All analyses will be stratified according to baseline tumor burden. A baseline variable is defined as the latest pre-treatment measure or information within a variable-specific window as specified in the SAP.

Demographic and baseline clinical characteristics will be tabulated. Dose and duration of lenalidomide and other relevant concomitant medications will be described. The proportion of patients with high tumor burden at baseline will be estimated with its two-sided 95% CI. In this study, high tumor burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.

Tumor flare reaction is an AE that presents with painful lymph nodes and/or painful spleen enlargement, and can be accompanied by fever, rash, or lymphocytosis. Early death is defined as any death occurring within 20 weeks of the initial administration of lenalidomide. The cumulative incidence rate of TFR and the proportion of early deaths (both with their exact two-sided 95% CIs) will be calculated.

The frequency of TFR and other adverse events related to lenalidomide collected and not listed in the current EU Summary of Product Characteristics (SmPC) will also be reported in summary tables. Because TFR occurs early in the course of treatment, any TFR events will be descriptively reported for up to 6 months of treatment. Tumor flare reaction will be characterized by clinical assessments and laboratory tests, and tabulated by frequency, severity, seriousness,

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time to onset, treatment outcome (treatment discontinuation, dose interruption or dose reduction), time to resolution, and relationship to lenalidomide and tumor burden.

In time to event analyses, cumulative incidence rates for TFR and death will be estimated using the Kaplan-Meier (KM) method. Since data is being collected retrospectively, the number of time points each patient may have will be unknown *a priori*. Given that the precision of the KM method varies with the number of time points available for analysis and that TFR is likely to occur early in treatment with lenalidomide (time to TFR is less than 5 days for almost 25% of patients experiencing TFR and the interquartile range for time to TFR in Study MCL-002 was [0.7, 2.4] weeks [Trněný, 2016]), there will likely be an impact on the precision of the estimate using this method.

As a consequence, KM analyses will not be performed as primary but as complementary analyses.

For KM analyses, the censoring rules applying to patients for whom the event was not observed during the 6-month period following the first lenalidomide dose will be the following:

- Any patient for whom information may exist in the source database after the 6-month period following the first lenalidomide dose will be censored at 6 months.
- Any patient for whom no information exists in the source database after the 6-month period following the first lenalidomide dose will be censored at the date of the last information available in the 6-month period.

Exploration of factors associated with TFR and with early death will be conducted in multivariate analyses.

9.8. Quality Control

All data collected for the MCL PASS should be recorded accurately.

Security of the data will be maintained at all times in line with applicable local law and procedures. Access will be limited to authorized individuals. Controls, such as document encryption, will be used to ensure the authenticity, integrity, and confidentiality of electronic records when transmitted over open systems (eg, the internet). Adequate back up of the data will be maintained throughout the course of the study.

The following activities aim to ensure data quality by checking the accuracy of the data collected from medical charts, checking the completeness and validity of data in the electronic data capture (EDC) through:

- Monitoring:
  - Performing source data verification (samples rather than 100%) to ensure EDC data match source data
- Data Management:
  - Using edit checks mainly within the EDC system for more efficient data cleaning and for identification of critical missing data, required data fields, illogical, and inconsistent data

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9.9. Limitations of the Research Methods

All AEs (as documented in the medical charts) collected in the study that are related to lenalidomide but not listed in the current EU SmPC will be summarized and frequencies calculated. Since the study is designed with TFR as the main outcome, it may not be sufficiently powered to provide a precise estimate for these adverse reactions. However, events captured through the review of medical records will be an improvement on spontaneous reporting as these events may not have been captured through normal channels.

Although a multivariate model will be attempted to explore the relationship between TFR and early death, the sample size may not be sufficiently powered and interpretation of results should be limited to hypothesis generation. There are also limitations to the Kaplan-Meier analysis as the retrospective nature of the study and the secondary use of the data may not allow for all the information needed with appropriate time precision and correspondence with the expected time to these events.

9.10. Other Aspects

Not applicable.

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10. PROTECTION OF HUMAN SUBJECTS

Data will be collected from patients who have given their informed consent or, in case it's not applicable, data will be collected in accordance with local legislation. For patients who have died and therefore cannot provide consent, local requirements will be followed.

This study will complete all regulatory and ethical review requirements in accordance with applicable regulations.

Given that this is a non-interventional study, it does not give rise to additional risks for the safety of the patients.

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11. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

This R/R MCL study is based upon secondary use of data. Reporting requirements for this non-interventional study are described in Module VI of the European Medicines Agency (EMA) Guideline on Good Pharmacovigilance Practices (GVP). Module VI (EMA, 2016) provides that "For non-interventional study designs which are based on secondary use of data, adverse reactions reporting is not required. Reports of adverse events/reactions should only be summarized in the study report, where applicable."

In addition to the information relevant to the primary objective, information on AEs related to lenalidomide and not listed in the current EU SmPC (Revlimid SmPC Section 4.8) will be collected. Common Terminology Criteria for Adverse Events (CTCAE) will be used to identify the incidence, but not the severity of the identified AEs as the study is based on retrospective data collection. The CTCAE will be used where feasible to provide a common definitional framework for the AEs collected as part of this study.

As required by the GVP modules for Periodic Safety Update Reports (PSURs) (Module VII [EMA, 2013]) and RMPs (Module V [EMA, 2016]), information on collected AEs related to lenalidomide will be included in the study report and reported appropriately in both the PSUR and the RMP. In cases of doubt, the reporting requirements will be clarified with the authorities concerned of the EU Member States.

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12. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

Regular safety updates will be made as per regulatory requirements via the PSURs. Interim analysis communications may be pursued if medical need arises.

Final data will be appropriately communicated when available, through presentation at major European or global congresses of hematology and/or oncology. Final results of the R/R MCL PASS also will be submitted for publication to an appropriate scientific and medical journal. Authorship will be based on scientific contribution to the study design and on enrollment of evaluable patients.

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ANNEX 1. LIST OF STAND-ALONE DOCUMENTS

None.

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ANNEX 2. ENCEPP CHECKLIST FOR STUDY PROTOCOLS

Doc.Ref. EMA/540136/2009

• ENCePP Checklist for Study Protocols (Revision 4)

Adopted by the ENCePP Steering Group on 15/10/2018

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) welcomes innovative designs and new methods of research. This Checklist has been developed by ENCePP to stimulate consideration of important principles when designing and writing a pharmacoepidemiological or pharmacovigilance study protocol. The Checklist is intended to promote the quality of such studies, not their uniformity. The user is also referred to the ENCePP Guide on Methodological Standards in Pharmacoepidemiology, which reviews and gives direct electronic access to guidance for research in pharmacoepidemiology and pharmacovigilance.

For each question of the Checklist, the investigator should indicate whether or not it has been addressed in the study protocol. If the answer is "Yes", the section number of the protocol where this issue has been discussed should be specified. It is possible that some questions do not apply to a particular study (for example, in the case of an innovative study design). In this case, the answer 'N/A' (Not Applicable) can be checked and the "Comments" field included for each section should be used to explain why. The "Comments" field can also be used to elaborate on a "No" answer.

This Checklist should be included as an Annex by marketing authorisation holders when submitting the protocol of a non-interventional post-authorisation safety study (PASS) to a regulatory authority (see the Guidance on the format and content of the protocol of non-interventional post-authorisation safety studies). The Checklist is a supporting document and does not replace the format of the protocol for PASS presented in the Guidance and Module VIII of the Good pharmacovigilance practices (GVP).

Study title:

EU PAS Register® number: **Study reference number (if applicable):**

Section 1: Milestones	**Yes**	**No**	**N/A**	**Section Number**
1.1 Does the protocol specify timelines for				6
1.1.1 Start of data collection[2]	☒	☐	☐	
1.1.2 End of data collection[3]	☒	☐	☐	

[2] Date from which information on the first study is first recorded in the study dataset or, in the case of secondary use of data, the date from which data extraction starts.

[3] Date from which the analytical dataset is completely available.

Section 1: Milestones	**Yes**	**No**	**N/A**	**Section Number**
1.1.3 Progress report(s)	☒	☐	☐	
1.1.4 Interim report(s)	☐	☒	☐	
1.1.5 Registration in the EU PAS Register®	☒	☐	☐	
1.1.6 Final report of study results.	☒	☐	☐	

Comments:

Section 2: Research question	**Yes**	**No**	**N/A**	**Section Number**
2.1 Does the formulation of the research question and objectives clearly explain:	☒	☐	☐	7,8
2.1.1 Why the study is conducted? (e.g. to address an important public health concern, a risk identified in the risk management plan, an emerging safety issue)	☒	☐	☐	
2.1.2 The objective(s) of the study?	☒	☐	☐	
2.1.3 The target population? (i.e. population or subgroup to whom the study results are intended to be generalised)	☒	☐	☐	
2.1.4 Which hypothesis(-es) is (are) to be tested?	☐	☒	☐	
2.1.5 If applicable, that there is no *a priori* hypothesis?	☐	☐	☒	

Comments:

These is no hypothesis testing therefore there is no a prior hypothesis

Section 3: Study design	**Yes**	**No**	**N/A**	**Section Number**
3.1 Is the study design described? (e.g. cohort, case-control, cross-sectional, other design)	☒	☐	☐	9.1
3.2 Does the protocol specify whether the study is based on primary, secondary or combined data collection?	☒	☐	☐	9.1, 9.4
3.3 Does the protocol specify measures of occurrence? (e.g., rate, risk, prevalence)	☒	☐	☐	9.7

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Section 3: Study design	**Yes**	**No**	**N/A**	**Section Number**
3.4 Does the protocol specify measure(s) of association? (e.g. risk, odds ratio, excess risk, rate ratio, hazard ratio, risk/rate difference, number needed to harm (NNH))	☐	☒	☐	
3.5 Does the protocol describe the approach for the collection and reporting of adverse events/adverse reactions? (e.g. adverse events that will not be collected in case of primary data collection)	☒	☐	☐	11

Comments:

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Section 4: Source and study populations		**Yes**	**No**	**N/A**	**Section Number**
4.1	Is the source population described?	☒	☐	☐	9.4
4.2	Is the planned study population defined in terms of:				9.1-9.4
	4.2.1 Study time period	☒	☐	☐	
	4.2.2 Age and sex	☐	☒	☐	
	4.2.3 Country of origin	☐	☒	☐	
	4.2.4 Disease/indication	☒	☐	☐	
	4.2.5 Duration of follow-up	☒	☐	☐	
4.3	Does the protocol define how the study population will be sampled from the source population? (e.g. event or inclusion/exclusion criteria)	☒	☐	☐	9.1

Comments:

Section 5: Exposure definition and measurement		**Yes**	**No**	**N/A**	**Section Number**
5.1	Does the protocol describe how the study exposure is defined and measured? (e.g. operational details for defining and categorising exposure, measurement of dose and duration of drug exposure)	☒	☐	☐	9.1-9.3
5.2	Does the protocol address the validity of the exposure measurement? (e.g. precision, accuracy, use of validation sub-study)	☐	☒	☐	
5.3	Is exposure categorised according to time windows?	☐	☒	☐	
5.4	Is intensity of exposure addressed? (e.g. dose, duration)	☐	☒	☐	
5.5	Is exposure categorised based on biological mechanism of action and taking into account the pharmacokinetics and pharmacodynamics of the drug?	☐	☒	☐	
5.6	Is (are) (an) appropriate comparator(s) identified?	☐	☐	☒	

Comments:

The aim of the study is to quantify the outcomes of interest and not a comparative study

Section 6: Outcome definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
6.1 Does the protocol specify the primary and secondary (if applicable) outcome(s) to be investigated?	☒	☐	☐	8
6.2 Does the protocol describe how the outcomes are defined and measured?	☒	☐	☐	9.1-9.3
6.3 Does the protocol address the validity of outcome measurement? (e.g. precision, accuracy, sensitivity, specificity, positive predictive value, use of validation sub-study)	☐	☒	☐	
6.4 Does the protocol describe specific outcomes relevant for Health Technology Assessment? (e.g. HRQoL, QALYs, DALYS, health care services utilisation, burden of disease or treatment, compliance, disease management)	☐	☒	☐	

Comments:

Section 7: Bias	**Yes**	**No**	**N/A**	**Section Number**
7.1 Does the protocol address ways to measure confounding? (e.g. confounding by indication)	☐	☒	☐	
7.2 Does the protocol address selection bias? (e.g. healthy user/adherer bias)	☐	☐	☒	
7.3 Does the protocol address information bias? (e.g. misclassification of exposure and outcomes, time-related bias)	☐	☐	☒	

Comments:

This study is designed to measure the rate of events in outcomes of interest in patients exposure to lenalidomide therefore selection bias and information bias are not applicable here.

Section 8: Effect measure modification	**Yes**	**No**	**N/A**	**Section Number**
8.1 Does the protocol address effect modifiers? (e.g. collection of data on known effect modifiers, sub-group analyses, anticipated direction of effect)	☐	☐	☒	

Comments:

This is not a comparative study therefore no measures of effect will be estimated and

effect modifiers are not relevant.

Section 9: Data sources	**Yes**	**No**	**N/A**	**Section Number**
9.1 Does the protocol describe the data source(s) used in the study for the ascertainment of:				
9.1.1 Exposure? (e.g. pharmacy dispensing, general practice prescribing, claims data, self-report, face-to-face interview)	☒	☐	☐	9.4
9.1.2 Outcomes? (e.g. clinical records, laboratory markers or values, claims data, self-report, patient interview including scales and questionnaires, vital statistics)	☒	☐	☐	9.4
9.1.3 Covariates and other characteristics?	☒	☐	☐	9.4
9.2 Does the protocol describe the information available from the data source(s) on:				
9.2.1 Exposure? (e.g. date of dispensing, drug quantity, dose, number of days of supply prescription, daily dosage, prescriber)	☐	☒	☐	
9.2.2 Outcomes? (e.g. date of occurrence, multiple event, severity measures related to event)	☐	☒	☐	
9.2.3 Covariates and other characteristics? (e.g. age, sex, clinical and drug use history, co-morbidity, co-medications, lifestyle)	☐	☒	☐	
9.3 Is a coding system described for:				
9.3.1 Exposure? (e.g. WHO Drug Dictionary, Anatomical Therapeutic Chemical (ATC) Classification System)	☐	☒	☐	
9.3.2 Outcomes? (e.g. International Classification of Diseases (ICD), Medical Dictionary for Regulatory Activities (MedDRA))	☐	☒	☐	
9.3.3 Covariates and other characteristics?	☐	☒	☐	
9.4 Is a linkage method between data sources described? (e.g. based on a unique identifier or other)	☐	☒	☐	

Comments:

Section 10: Analysis plan	**Yes**	**No**	**N/A**	**Section Number**
10.1 Are the statistical methods and the reason for their choice described?	☒	☐	☐	9.7
10.2 Is study size and/or statistical precision estimated?	☒	☐	☐	9.5

Section 10: Analysis plan	**Yes**	**No**	**N/A**	**Section Number**
10.3 Are descriptive analyses included?	☒	☐	☐	9.7
10.4 Are stratified analyses included?	☐	☐	☒	
10.5 Does the plan describe methods for analytic control of confounding?	☐	☐	☒	
10.6 Does the plan describe methods for analytic control of outcome misclassification?	☐	☐	☒	
10.7 Does the plan describe methods for handling missing data?	☐	☐	☒	
10.8 Are relevant sensitivity analyses described?	☐	☒	☐	

Comments:

Given the goal of the study is to estimate the rate of outcome event and not a comparative study, items 10.4-10.7 does not apply.

Section 11: Data management and quality control	**Yes**	**No**	**N/A**	**Section Number**
11.1 Does the protocol provide information on data storage? (e.g. software and IT environment, database maintenance and anti-fraud protection, archiving)	☒	☐	☐	
11.2 Are methods of quality assurance described?	☒	☐	☐	
11.3 Is there a system in place for independent review of study results?	☐	☒	☐	

Comments:

Section 12: Limitations	**Yes**	**No**	**N/A**	**Section Number**
12.1 Does the protocol discuss the impact on the study results of:				
12.1.1 Selection bias?	☐	☒	☐	
12.1.2 Information bias?	☐	☐	☒	
12.1.3 Residual/unmeasured confounding? (e.g. anticipated direction and magnitude of such biases, validation sub-study, use of validation and external data, analytical methods).	☐	☐	☒	

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Section 12: Limitations	**Yes**	**No**	**N/A**	**Section Number**
12.2 Does the protocol discuss study feasibility? (e.g. study size, anticipated exposure uptake, duration of follow-up in a cohort study, patient recruitment, precision of the estimates)	☒	☐	☐	9.9

Comments:

As the study is descriptive and no comparisons are conducted, information bias and confounding are not relevant.

Section 13: Ethical/data protection issues	**Yes**	**No**	**N/A**	**Section Number**
13.1 Have requirements of Ethics Committee/ Institutional Review Board been described?	☐	☒	☐	
13.2 Has any outcome of an ethical review procedure been addressed?	☒	☐	☐	10
13.3 Have data protection requirements been described?	☒	☐	☐	10

Comments:

Section 14: Amendments and deviations	**Yes**	**No**	**N/A**	**Section Number**
14.1 Does the protocol include a section to document amendments and deviations?	☒	☐	☐	5

Comments:

Section 15: Plans for communication of study results	**Yes**	**No**	**N/A**	**Section Number**
15.1 Are plans described for communicating study results (e.g. to regulatory authorities)?	☒	☐	☐	12
15.2 Are plans described for disseminating study results externally, including publication?	☒	☐	☐	12

Comments:

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Name of the main authors of the protocol: [redacted]

Date: 28 Aug 2019

Signature: [redacted]

Date: 28 Aug 2019

Signature: [redacted]

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ANNEX 3. ADDITIONAL INFORMATION

Not applicable.

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Celgene Signing Page

This is a representation of an electronic record that was signed electronically in Livelink. This page is the manifestation of the electronic signature(s) used in compliance with the organizations electronic signature policies and procedures.

UserName: [redacted]
Title: Executive Director II, GDSRM International
Date: Friday, 06 September 2019, 11:56 AM Eastern Daylight Time
Meaning: Approved, no changes necessary.
==========

UserName: [redacted]
Title: CVP, Global Medical Affairs
Date: Friday, 06 September 2019, 05:38 PM Eastern Daylight Time
Meaning: Approved, no changes necessary.
==========

Title	A Non-interventional, Post-authorization Safety Study of Patients with Relapsed or Refractory Mantle Cell Lymphoma to Further Investigate and Characterize the Association of Lenalidomide With Tumor Flare Reaction and High Tumor Burden
Protocol version identifier	CC-5013-MCL-005 (Version 3.0)
Date of last version of protocol	27 Mar 2017
EU PAS register number	To Be Confirmed
Active substance	Lenalidomide (ATC code: L04AX04)
Medicinal product	Revlimid®
Product reference	EU/1/07/391/001-009
Procedure number	EMEA/H/C/000717/II/79
Marketing authorization holder	Celgene Europe Limited
Joint PASS	No
Research question and objectives	This study is designed as a retrospective non-interventional study of patients with relapsed or refractory (R/R) mantle cell lymphoma (MCL) to further investigate the following objectives: Primary Objective To quantify and characterize the event of tumor flare reaction (TFR) by tumor burden (assessed based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting. Secondary Objective To quantify and characterize the proportion of early deaths (defined as deaths within 20 weeks of the initial administration of lenalidomide) by tumor burden in R/R MCL patients treated with lenalidomide in a real-world setting.
Countries of study	The study comprises two cohorts. For Cohort 1, MCL patients in the Nordic countries (*inter alia*, Denmark and Sweden) will be identified through electronic medical records (EMRs), which contain information on laboratory values, pathology/radiology results, hospital administered drugs, adverse events, and disease progression, ie, enabling identification of R/R MCL patients. The cohort identified through EMRs at chosen hospitals will then be linked to the national health registries. Exposure to lenalidomide will be identified through prescription registers or medical chart review, depending on dispensing pattern in the particular Nordic country.

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	For Cohort 2, sites will be identified in other European countries (*inter alia* Germany) where patients have been treated with lenalidomide for R/R MCL. Identification of sites will be completed through partnership with the European Mantle Cell Lymphoma (European MCL) Registry and in addition, sites will be identified by Celgene. Identified sites will then be assessed for feasibility and invited to participate in the R/R MCL PASS. For both cohorts, only sites where lenalidomide treatment for R/R MCL is reimbursed will be selected for the study.
Authors	[redacted]

Marketing Authorization Holder(s)

Marketing authorization holder	[redacted]
MAH contact person	[redacted]

CONFIDENTIAL

This protocol is provided to you as an Investigator, potential Investigator, or consultant for review by you, your staff, and ethics committee/institutional review board. The information contained in this document is regarded as confidential and, except to the extent necessary to obtain informed consent, may not be disclosed to another party unless such disclosure is required by law or regulations. Persons to whom the information is disclosed must be informed that the information is confidential and may not be further disclosed by them.

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SIGNATURE PAGE

{See appended electronic signature page}

_____

Signature of Celgene Therapeutic Area Head

[redacted]

Printed Name of Celgene Therapeutic Area Head

Date Signed _____

{See appended electronic signature page}

_____

Signature of Celgene Qualified Person for Pharmacovigilance

[redacted]

Printed Name of Qualified Person for Pharmacovigilance

Date Signed _____

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2. LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse event
CHMP	Committee for Medicinal Products for Human Use
CI	Confidence interval
CLL	Chronic lymphocytic leukemia
CRO	Contract research organization
CTCAE	Common Terminology Criteria for Adverse Events
EC	European Commission
ECOG PS	Eastern Cooperative Oncology Group Performance Status
eCRF	Electronic case report form
EDC	Electronic data capture
EMA	European Medicines Agency
EMR	Electronic medical record
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EU	European Union
GVP	Good Pharmacovigilance Practices
HR	Hazard ratio
ICF	Informed consent form
IMiD®	IMiDs are a proprietary series of drugs with immunomodulatory and other properties
IQR	Interquartile range
MAH	Marketing authorization holder
MCL	Mantle cell lymphoma
MDS	Myelodysplastic syndrome
MM	Multiple myeloma
NDMCL	Newly diagnosed mantle cell lymphoma
NHL	Non-Hodgkin's lymphoma
NIS	Non-interventional study
PAS	Post-authorization study
PASS	Post-authorization safety study
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan

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Abbreviation	Definition
R/R	Relapsed or refractory
SAE	Serious adverse event
SAP	Statistical analysis plan
SmPC	Summary of Product Characteristics
TEAE	Treatment-emergent adverse event
TFR	Tumor flare reaction
UN	United Nation
US	United States

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3. RESPONSIBLE PARTIES

For inquiries regarding this post-authorization safety study (PASS) protocol in relapsed or refractory mantle cell lymphoma (R/R MCL), contact information is provided in Table 1.

Table 1: Contact Information for Operational Inquiries

Sponsor:	[redacted]
Contract Research Organization (CRO):	[redacted]
CRO Study Manager:	[redacted]
Celgene Study Manager:	[redacted]
Celgene Physician:	[redacted]

CRO = contract research organization.

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4. ABSTRACT

Title: A Non-interventional, Post-authorization Safety Study of Patients with Relapsed or Refractory Mantle Cell Lymphoma to Further Investigate and Characterize the Association of Lenalidomide With Tumor Flare Reaction and High Tumor Burden

Rationale and background:

In the European Union (EU), the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion on 28 Jan 2016 for the use of lenalidomide in the treatment of adult patients with relapsed or refractory mantle cell lymphoma. The European Commission (EC) granted a marketing authorization for this indication on 08 Jul 2016.

While the marketing authorization was granted, the Pharmacovigilance Risk Assessment Committee (PRAC) review of the Risk Management Plan (RMP) led to a request for further assessment of safety issues via postmarketing surveillance. This relapsed or refractory mantle cell lymphoma (R/R MCL) post-authorization safety study (PASS) will gather additional safety information as a multinational, non-interventional study (NIS) to further investigate the primary and secondary objectives described below.

Research question and objectives:

This study is designed as a retrospective non-interventional study of patients with R/R MCL to further investigate the following objectives:

Primary Objective

To quantify and characterize the event of tumor flare reaction (TFR) by tumor burden (assessed based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting.

Secondary Objective

To quantify and characterize the proportion of early deaths (defined as deaths within 20 weeks of the initial administration of lenalidomide) by tumor burden in R/R MCL patients treated with lenalidomide in a real-world setting.

Study design:

This is a European multinational, retrospective, non-interventional study of patients with R/R MCL.

The proposed study has two cohorts:

For Cohort 1, MCL patients in the Nordic countries (*inter alia*, Denmark and Sweden) will be identified through electronic medical records (EMRs), which contain information on laboratory values, pathology/radiology results, hospital administered drugs, adverse events, and disease progression, ie, enabling identification of R/R MCL patients. The cohort identified through EMRs at chosen hospitals will then be linked to the national health registries.

Exposure to lenalidomide will be identified through prescription registers or medical chart review, depending on dispensing pattern in the particular Nordic country.

For Cohort 2, sites will be identified in other European countries (*inter alia* Germany) where patients have been treated with lenalidomide for R/R MCL. Identification of sites will be completed through partnership with the European Mantle Cell Lymphoma (European MCL) Registry, and in addition, sites

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will be identified by Celgene. Identified sites will then be assessed for feasibility and invited to participate in the R/R MCL PASS.

For both cohorts, only sites where lenalidomide treatment for R/R MCL is reimbursed will be selected for the study.

All data will be collected retrospectively from identified patients following the first dose of lenalidomide treatment for up to 6 months including those patients who died within this data collection period.

A common set of key variables will be extracted in accordance with the study objectives from the medical records of eligible MCL patients for both cohorts of the study.

Population:

The study population will consist of a retrospective cohort of R/R MCL patients who have commenced treatment with lenalidomide after 08 Jul 2016 (date EC marketing authorization was granted).

Inclusion Criteria:

1) Received at least one dose of lenalidomide commencing after 08 Jul 2016 for the treatment of R/R MCL.
2) Informed consent of the patient or an authorized third person or authority, if required by law, given prior to data collection.
3) Patient must be ≥18 years of age at the time of signing the informed consent form (ICF).

Exclusion Criteria:

1) Patients will be excluded if they were participating in an interventional clinical trial during the treatment period under observation in this PASS.

Recruitment will continue until at least 560 R/R MCL patients exposed to lenalidomide are included in the study.

Variables:

Variables to be evaluated in this study include baseline demographic and clinical variables (the *"population dataset"*), treatment variables related to lenalidomide use and other relevant medications (the *"treatment dataset"*), and the outcome variables for safety (the *"outcomes dataset"*).

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Data sources:

Cohort 1: Retrospective data collection from Nordic registries and national health databases

MCL patients in the Nordic countries (*inter alia*, Denmark and Sweden) will be identified through electronic medical records (EMRs), which contain information on laboratory values, pathology/radiology results, hospital administered drugs, adverse events, and disease progression, ie, enabling identification of R/R MCL patients. The cohort identified through EMRs at chosen hospitals will then be linked to the national health registries. The national personal identity numbers assigned to each individual at birth or immigration enables linkage between various data sources, including the Cancer Registry, Patient Registry, Prescription Registry (pharmacy database), Mortality Registry. These registries contain information on demographics, patient care within in-patient and out-patient settings, comorbidities, health care resource usage, drug usage history, and cause of death. The linkage to the previously mentioned registries will be established for meeting the study objectives.

Exposure to lenalidomide will be identified through prescription registers or medical chart review, depending on dispensing pattern in the particular Nordic country.

Cohort 2: Retrospective data collection from sites

Sites where R/R MCL patients have been treated with lenalidomide will be identified in two ways via:

a) European MCL Registry

- The European MCL Registry is a multinational registry that collects medical history and treatment information on MCL patients. Sites where patients have been treated with lenalidomide for R/R MCL will be identified through the European MCL Registry. Sites are expected to participate in Germany, and in other countries where the European MCL Registry is active and where lenalidomide is reimbursed. The network will cover a population of approximately 150 million people. The European MCL Registry will identify sites with eligible patients and notify Celgene of these sites.

b) Celgene interactions with known MCL-treating sites

- Sites will also be identified by Celgene and will be approached directly once lenalidomide is reimbursed to assess the feasibility of study participation.

All sites, once identified, will be contacted to participate in the study by a contract research organization (CRO) representing Celgene. Once a site agrees to participate, data will be collected retrospectively regarding the identified patients following the first dose of lenalidomide treatment for up to 6 months, including those patients who died within this data collection period.

A common set of key variables will be collected for both cohorts of the study.

Study size:

The incidence of newly diagnosed MCL (NDMCL) is 0.45 cases per 100,000 per year (Sant, 2010). With a population of 738,442,000 in Europe in 2015 (United Nations [UN] estimate), the number of NDMCL cases per year is estimated at 3,323. Of these, 67% are expected to be relapsed or refractory resulting in 2,226 R/R MCL cases per year (3,323 x 0.67).

Assuming a 10% use of lenalidomide as second-line treatment in these patients by 2018 results in an estimated 223 cases per year (2,226 x 0.10). Assuming that 60% of R/R MCL patients receive second-line

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treatment and that 25% of these receive third-line lenalidomide treatment by 2018 leads to an estimated 334 cases (2,226 x 0.6 x 0.25). This then gives an estimated 557 (223 + 334) cases per year of R/R MCL patients receiving second- or third-line lenalidomide treatment.

Sample size required for estimation of the cumulative incidence of TFR

Sample size calculation is based upon the observed cumulative incidence of TFR (9.6%) in the CC-5013-MCL-002 study of 167 R/R MCL patients treated with lenalidomide with an exact two-sided 95% CI = (5.6%; 15.1%). From the CC-5013-MCL-002 study, there is a 20% chance that the cumulative incidence of TFR would exceed 12.0% (upper limit of the one-sided 80% CI).

Under the assumption of a true TFR cumulative incidence rate of 9.6%, 497 patients are needed for reaching a precision of +3% on the estimate of the TFR cumulative incidence rate (upper limit of the exact two-sided 95% CI).

A sample size of 558 is required should the observed incidence of TFR reach 12% in the study population. This would give a precision of +3% based on the upper limit of the exact two-sided 95% CI. Therefore, a sample size of 560 patients will be targeted.

Estimation of early death rate

In Study CC-5013-MCL-002, 13.2% (22/167) of lenalidomide-treated patients died early. The exact two-sided 95% CI was (8.4%; 19.3%), and there is only a 20% chance that the early death rate would exceed 15.9% (upper limit of the one-sided 80% CI).

With 560 patients, the study will allow a calculation of the early death rate with a precision of +3.1% for the upper limit of the exact two-sided 95% CI if the observed rate is 13.2%, and +3.4% if it is 15.9%.

Based on market projections for lenalidomide in R/R MCL patients in Europe, the proposed study will need to accrue patients for 8 years.

Data analysis:

The analysis will be descriptive and no *a priori* hypotheses will be tested. A statistical analysis plan (SAP) will be developed for this study. All analyses will be stratified according to baseline tumor burden.

Demographic and baseline clinical characteristics will be tabulated. Dose and duration of lenalidomide and other relevant concomitant medications will be described. The proportion of patients with high tumor burden at baseline will be estimated with its two-sided 95% CI. In this study, high tumor burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.

Tumor flare reaction is an AE that presents with painful lymph nodes and/or painful spleen enlargement, and can be accompanied by fever, rash, or lymphocytosis. Early death is defined as any death occurring within 20 weeks of the initial administration of lenalidomide. The cumulative incidence of TFR and early death (both with their exact two-sided 95% CIs) will be calculated.

The frequency of TFR and other adverse events related to lenalidomide collected and not listed in the current EU Summary of Product Characteristics (SmPC) will also be reported in summary tables. Because TFR occurs early in the course of treatment, any TFR events will be descriptively reported for up to 6 months of treatment. Tumor flare reaction will be characterized by clinical assessments and laboratory tests, and tabulated by frequency, severity, seriousness, time to onset, treatment outcome (treatment

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discontinuation, dose interruption or dose reduction), time to resolution, and relationship to lenalidomide and tumor burden.

Time to event analyses and incidence rates for TFR and early death will be estimated using the Kaplan-Meier (KM) method. Since data is being collected retrospectively, the number of time points each patient may have will be unknown *a priori*. Given that the precision of the KM method varies with the number of time points available for analysis and that TFR is likely to occur early in treatment with lenalidomide (time to TFR is less than 5 days for almost 25% of patients experiencing TFR and the interquartile range for time to TFR in Study MCL-002 was [0.7, 2.4] weeks [Trněný, 2016]), there will likely be an impact on the precision of the estimate using this method.

As a consequence, KM analyses will not be performed as primary but as complementary analyses.

For KM analyses, the censoring rules applying to patients for whom the event was not observed during the 6-month period following the first lenalidomide dose will be the following:

- Any patient for whom information may exist in the source database after the 6-month period following the first lenalidomide dose will be censored at 6 months.
- Any patient for whom no information exists in the source database after the 6-month period following the first lenalidomide dose will be censored at the date of the last information available in the 6-month period.

Exploration of factors associated with TFR and with early death will be conducted in multivariate analyses.

Milestones:

- Estimated start of data collection: Q2 2018
- Estimated end of data collection: Q4 2026
- Study progress reports:
  - With annual Periodic Safety Update Reports (PSURs)
- Registration in the EU post-authorization study (PAS) register: To be confirmed
- Final report of study results: Q4 2027

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5. AMENDMENTS AND UPDATES

None

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6. MILESTONES

Milestones for this study are summarized in Table 2.

Table 2: Study Milestones

Milestone	Planned Date
Estimated Start of Data Collection	Q2 2018
Estimated End of Data Collection	Q4 2026
Study Progress Reports	
PSUR	Annual as per PSUR cycle
Registration in the EU PAS Registry	To be confirmed
Final Report of Study Results	Q4 2027

EU = European Union; PAS = post-authorization study; PSUR = Periodic Safety Update Report; Q2 = second quarter; Q4 = fourth quarter.

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7. RATIONALE AND BACKGROUND

7.1. Rationale

Lenalidomide is a member of a proprietary series of drugs with immunomodulatory and other properties, referred to as IMiDs®[1].

In the United States (US), lenalidomide received regulatory approval on 05 Jun 2013, for the treatment of patients with mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib. In the European Union (EU), the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion on 28 Jan 2016 for the use of lenalidomide in the treatment of adult patients with relapsed or refractory mantle cell lymphoma. The European Commission (EC) granted a marketing authorization for this indication on 08 Jul 2016.

While the marketing authorization was granted, the Pharmacovigilance Risk Assessment Committee (PRAC), after reviewing the Risk Management Plan (RMP), requested further assessment of safety issues via postmarketing surveillance. This relapsed or refractory (R/R) MCL PASS will aim to gather additional safety information as a multinational, non-interventional study (NIS) to further investigate the research objectives described in Section 8.2.

7.2. Background

Mantle cell lymphoma is a type of non-Hodgkin's lymphoma (NHL), a heterogeneous group of lymphoproliferative malignancies with differing clinical features and responses to treatment (Armitage, 1993). The annual incidence of MCL in Europe was estimated as 0.45 cases per 100,000 persons based on cancer registry data from 20 countries (Sant, 2010). Patients with MCL typically are predominantly male and Caucasian with a median age of > 60 years, and present with advanced stage disease. Despite intensive induction therapies in the front-line setting of young and fit patients, the clinical course is typically that of repeated relapses, and median survival of MCL is only 3 to 5 years (Abrahamsson, 2014; Salek, 2014).

7.2.1. Study CC-5013-MCL-002

Study CC-5013-MCL-002 (SPRINT; hereinafter Study MCL-002), ClinicalTrials.gov number: NCT00875667, was the main study and basis for the marketing authorization for the R/R MCL indication granted on 08 Jul 2016 by the EC.

Study MCL-002 was a randomized, Phase 2 study of patients with MCL aged 18 years or older at 67 clinics and academic centers in 12 countries who relapsed 1 to 2 times, had Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 to 2, at least 1 measurable lesion to be eligible, and who were ineligible for intensive chemotherapy or stem-cell transplantation.

Between 30 Apr 2009 and 07 Mar 2013, 254 patients were enrolled: 170 (67%) were randomly assigned to receive lenalidomide (Lenalidomide Arm), 84 (33%) to receive investigator's choice monotherapy (Control Arm). Patients had a median age of 68.5 years and received a median of

[1] IMiDs® are a proprietary series of drugs with immunomodulatory and other properties.

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2 previous regimens. With a median follow-up of 15.9 months, lenalidomide significantly improved progression-free survival compared with investigator's choice (median 8.7 months [95% confidence interval {CI}: 5.5, 12.1] versus 5.2 months [95% CI: 3.7, 6.9]) with a hazard ratio (HR) of 0.61 (95% CI: 0.44, 0.84; p = 0·004). In the 167 patients in the Lenalidomide Arm and 83 patients in the Control Arm who received at least one dose of treatment, the most common Grade 3 or 4 adverse events (AEs), respectively, included neutropenia (73 [44%] versus 28 [34%]) without increased risk of infection; thrombocytopenia (30 [18%] versus 23 [28%]); leucopenia (13 [8%] vs 9 [11%]); and anemia (14 [8%] vs 6 [7%]) (Trněný, 2016).

7.2.2. Tumor Flare Reaction in Study MCL-002

Tumor flare reaction is an AE that is associated with treatment of patients with lymphoma or chronic lymphocytic leukemia (CLL) with immunomodulatory drugs due to their specific mode of action, but not with chemotherapy (Andritsos, 2008; Chanan-Khan, 2006; Chanan-Khan, 2011a; Cheson, 2016; Corazzelli, 2010; Eve, 2010a; Ferrajoli, 2008a; Goy, 2013; Kayar, 2014; Witzig, 2011). It clinically presents with painful lymph nodes and/or spleen enlargement and can be accompanied by fever, rash, or lymphocytosis. Tumor flare reaction has been reported as a new important identified risk specific to lenalidomide treatment of CLL and B-cell lymphomas, but was not reported in association with the other target populations for Revlimid® (multiple myeloma [MM]; myelodysplastic syndrome [MDS]). Tumor flare reaction usually develops early in the course of therapy and may mimic progression of disease and subsides and resolves over time. Symptomatic treatment is used depending on the severity of the TFR.

In Study MCL-002, TFR was reported in the Lenalidomide Arm only (16 of 167 patients, [9.6%]) but not in the Control Arm (single-agent therapy with chemotherapy or rituximab). Of these 16 TFR events, the events in 3 (1.8%) subjects were classified as Grade 3 or 4 events (no Grade 5 AEs were reported): 1 event (0.6%) was a serious AE (SAE) (Celgene data on file) and 1 event (0.6%) resulted in treatment discontinuation. All TFR events occurred in Cycle 1 of treatment, except for 1 TFR event that started in Cycle 2. The median time to TFR was 1.1 weeks (interquartile range [IQR]: 0.7, 2.4) (Trněný, 2016).

The variables that remained in the final multivariate model in Study MCL-002, and were strongly and independently correlated with TFR, high Mantle Cell Lymphoma International Prognostic Index (MIPI) score at diagnosis (p = 0.084) and bulky disease at baseline (p = 0.020), appeared to be risk factors for TFR.

In Study MCL-002, no SAEs of TFR were observed in the group of subjects with high absolute lymphocyte count (> 15 g/L) at baseline. Therefore, these subjects do not seem to be at a particularly high risk for such events, supporting the analyses for TFR in which an elevated site blood cell count at baseline was not an independent risk factor for the occurrence of TFR.

In the Revlimid Summary of Product Characteristics (SmPC), TFR has been listed as an adverse drug reaction (Revlimid SmPC Section 4.8), added as a specific warning (Revlimid SmPC Section 4.4), and cited as an important identified risk in the RMP (Version 34, Section 3.11).

7.2.3. Tumor Burden and Early Deaths in Study MCL-002

In Study MCL-002, there was an overall risk reduction of 11% for the secondary endpoint overall survival (OS) when comparing the Lenalidomide Arm to the Control Arm (HR of 0.89 [95% CI, 0.62, 1.28]; p = 0.519, log-rank test). However, there was also an increase in deaths within 20 weeks from randomization (early deaths) in lenalidomide-treated patients (22/167 [13.2%]) in the Lenalidomide Arm versus 6/83 (7.2%) patients treated in the Control Arm.

It is important to note that there was an imbalance in important baseline disease-related risk factors between treatment arms, which disfavored subjects in the Lenalidomide Arm. This included high-risk MIPI scores, elevated levels of LDH, bulky disease, and high tumor burden, all of which were more frequently observed in the Lenalidomide Arm. The proportion of patients with high tumor burden (defined by at least one lesion 5 cm or more in diameter or three lesions 3 cm or more in diameter by central radiology review) in the Lenalidomide Arm was 81 (48%) of 170 patients versus 28 (33%) of 84 patients in the Control Arm (investigator's choice of monotherapy with either chlorambucil, cytarabine, rituximab, fludarabine, or gemcitabine) (Trněný, 2016).

Additional analyses were done to further characterize these early deaths with respect to disease-related characteristics. Based on a multivariate analysis, only high tumor burden at baseline was identified as a significant risk factor for early death. Treatment was not identified as a risk factor in the multivariate analysis.

The proportion of subjects with high tumor burden at baseline who died within 20 weeks (19.8% versus 7.1%) and within 52 weeks (39.5% versus 21.4%) after randomization was greater in the Lenalidomide Arm compared with the Control Arm (Celgene data on file).

In the Lenalidomide Arm, 11 (13.6%) of the 81 subjects who had high tumor burden at baseline discontinued treatment during Cycle 1 and the majority of these (7 of 11 subjects) did so due to treatment-emergent adverse events (TEAEs). In comparison, 4 (5.1%) of the 78 subjects who had low tumor burden at baseline discontinued treatment during Cycle 1; the majority of these (3 of 4 subjects) also discontinued treatment due to TEAEs (Celgene data on file).

In the Control Arm, 1 (3.6%) of the 28 subjects who had high tumor burden at baseline discontinued treatment during Cycle 1 (Celgene data on file).

Based on the above data, high tumor burden is a relevant factor for early death, regardless of treatment arm. However, it remains possible that the presence of TFR, an adverse event related to lenalidomide use, could have contributed to the early death in addition to high tumour burden. This hypothesis could not be tested given that there is no TFR case in the control group. It is unfortunate that in the MCL-002 study (Trněný, 2016), the protocol did not use tumor burden at baseline as a stratification factor.

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8. RESEARCH QUESTION AND OBJECTIVES

8.1. Research Question

This study is designed as a retrospective non-interventional study of patients with R/R MCL to further investigate the research objectives described in Section 8.2.

8.2. Research Objectives

8.2.1. Primary Objective

To quantify and characterize the event of TFR by tumor burden (assessed based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting.

8.2.2. Secondary Objective(s)

To quantify and characterize the proportion of early deaths (defined as deaths within 20 weeks of initial administration of lenalidomide) by tumor burden in R/R MCL patients treated with lenalidomide in a real-world setting.

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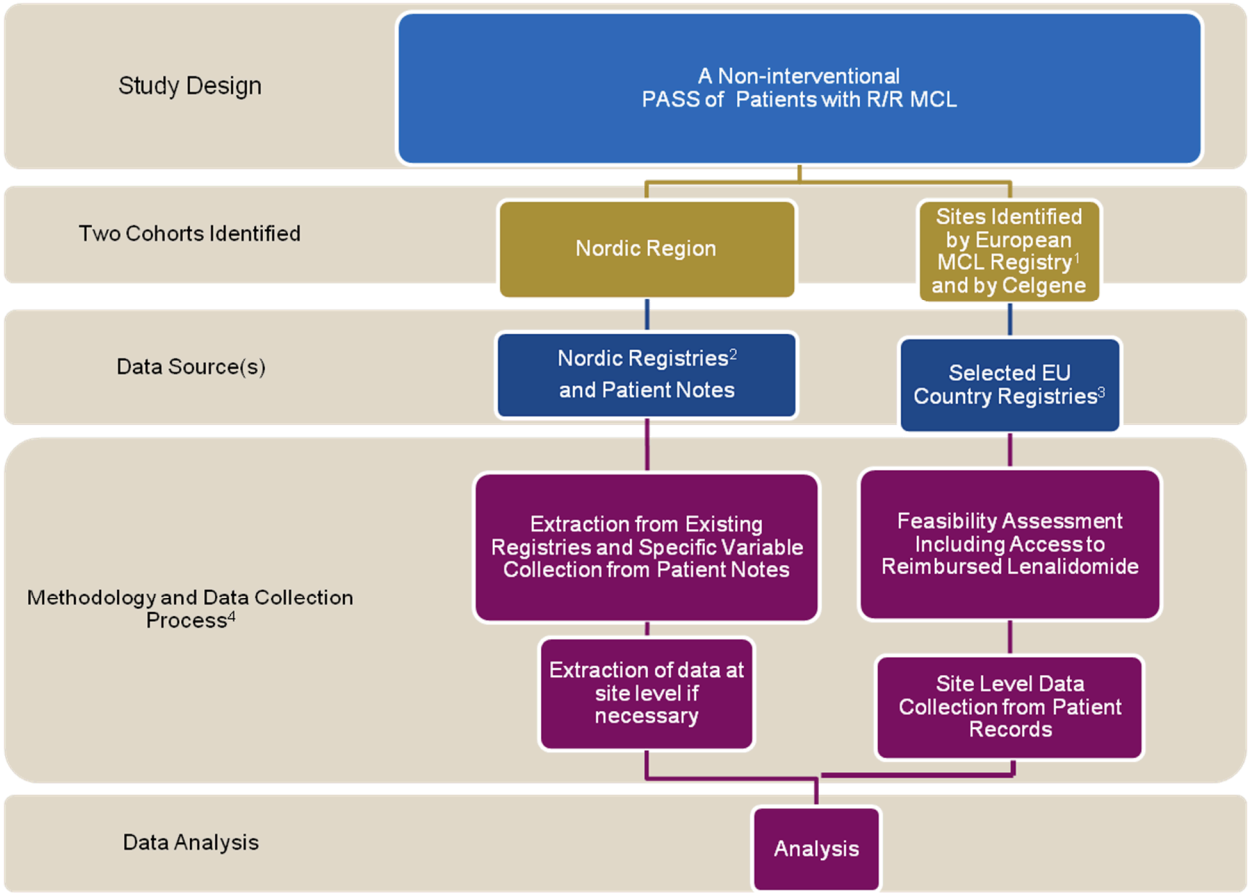
9. RESEARCH METHODS

9.1. Study Design and Selection Criteria

9.1.1. Study Design

This is a European multinational, retrospective, non-interventional study of patients with R/R MCL. Figure 1 provides a high-level schematic of the design of the study.

Figure 1: Study Design



EU = European Union; MCL = mantle cell lymphoma; PASS = post-authorization safety study; R/R = relapsed or refractory.

[1] European MCL Registry: European Mantle Cell Lymphoma Registry (on behalf of EU MCL Network) in collaboration with University of Mainz, Germany. Identification of sites will be completed through partnership with the European MCL Registry, and in addition, sites will be identified by Celgene.

[2] Nordic Registries: *inter alia*, Denmark and Sweden.

[3] In Germany, and in other countries where the European MCL Registry is active and where lenalidomide is reimbursed.

[4] A common set of key variables will be extracted from the medical records of eligible MCL patients.

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The proposed study has two cohorts.

For Cohort 1, MCL patients in the Nordic countries (*inter alia*, Denmark and Sweden) will be identified through electronic medical records (EMRs), which contain information on laboratory values, pathology/radiology results, hospital administered drugs, adverse events, and disease progression, ie, enabling identification of R/R MCL patients. The cohort identified through EMRs at chosen hospitals will then be linked to the national health registries.

Exposure to lenalidomide will be identified through prescription registers or medical chart review, depending on dispensing pattern in the particular Nordic country.

For Cohort 2, sites will be identified in other European countries (*inter alia* Germany) where patients have been treated with lenalidomide for R/R MCL. Identification of sites will be completed through partnership with the European Mantle Cell Lymphoma (European MCL) Registry, and in addition, sites will be identified by Celgene. Identified sites will then be assessed for feasibility and invited to participate in the R/R MCL PASS.

For both cohorts, only sites where lenalidomide treatment for R/R MCL is reimbursed will be selected for the study.

All data will be collected retrospectively from identified patients following the first dose of lenalidomide treatment for up to 6 months including those patients who died within this data collection period.

More details about the identification of sites and patients are provided in Section 9.4 (Data Sources) below.

A common set of key variables will be extracted in accordance with the study objectives from the medical records of eligible MCL patients for both cohorts of the study.

9.1.2. Selection Criteria

9.1.2.1. Inclusion Criteria

1) Received at least one dose of lenalidomide commencing after 08 Jul 2016 for the treatment of R/R MCL.
2) Informed consent of the patient or an authorized third person or authority, if required by law, given prior to data collection.
3) Patient must be ≥18 years of age at the time of signing the informed consent form (ICF).

9.1.2.2. Exclusion Criteria

1) Patients will be excluded if they were participating in an interventional clinical trial during the treatment period under observation in this PASS.

9.2. Setting

Study Population

The study population will consist of a retrospective cohort of R/R MCL patients who have commenced treatment with lenalidomide after 08 Jul 2016 (date marketing authorization was

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granted). Three datasets will be described for the study population and will form the basis of subsequent analyses:

- Population dataset
- Treatment dataset
- Outcomes dataset

9.3. Variables

Variables to be evaluated in this study include baseline demographic and clinical variables (*"population dataset"*) (Table 3), treatment variables related to lenalidomide use and other relevant medications (*"treatment dataset"*) (Table 4), and the outcome variables for safety (*"outcomes dataset"*) (Table 5).

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Table 3: Demographics and Clinical Variables

Variables	Data to be Collected
Demographics	
Age	Date of birth
Sex	Female/male
Clinical Variables	
Informed consent	Date of consent
MCL	Date of initial MCL diagnosis; MIPI score at initial diagnosis; Bulky Disease at initial diagnosis; Prior stem cell transplantation (autologous/allogeneic); Date of last relapse/disease progression before lenalidomide therapy; Time from last dose of last therapy before lenalidomide therapy
Medical history	Prior history of TFR; Cardiovascular events (eg, arrhythmia and coronary artery disease); Cerebrovascular events (eg, TIA and stroke); Thromboembolic events (arterial and venous [eg, DVT, PE, and MI]); Peripheral/autonomic neuropathy; Pulmonary, hepatic, renal disease; History of other malignant diseases; Other relevant concomitant diseases or medical conditions
Disease-related characteristics	Tumor burden (high tumor burden is defined as at least one lesion of ≥ 5 cm diameter or at least 3 lesions of ≥3 cm diameter); Bulky disease (≥7 cm) at beginning of lenalidomide treatment; ECOG performance status
Relevant Concomitant Medications related to TFR treatment and/or prophylaxis	Description of Concomitant Medication Indication of Concomitant Medication Start date of Concomitant Medication
Laboratory tests	Hematology: hemoglobin, platelets, WBC, ANC, ALC Biochemistry: LDH, creatinine, blood glucose, bilirubin, albumin, ALT, AST, calcium, phosphorus, sodium, potassium, CRP

ALC = absolute lymphocyte count; ALT = alanine aminotransferase; ANC = absolute neutrophil count; AST = aspartate aminotransferase; CRP = C-reactive protein; DVT = deep vein thrombosis; ECOG = Eastern Cooperative Oncology Group; LDH = lactic dehydrogenase; MCL = mantle cell lymphoma; MI = myocardial infarction; MIPI = Mantle Cell Lymphoma International Prognostic Index; PE = pulmonary embolism; TIA = transient ischemic attack; TFR = tumor flare reaction; WBC = white blood cell.

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Table 4: Lenalidomide Therapy and Other Treatment Variables

Variables	Data to be Collected
Previous treatments	Number of previous lines of treatment; Description of previous treatments
Lenalidomide treatment	(Date of start and end of treatment [dd/mm/yyyy], lenalidomide dose and regimen, reason for lenalidomide discontinuation or any interruption of therapy with lenalidomide, dose adjustments, where applicable)

Table 5: Outcome Variables for Safety

Variables	Data to be Collected
TFR (physician reported)	Adverse Event reported in eCRF/Medical file (onset date, stop date, severity, seriousness, clinical signs and symptoms, lab tests, treatment outcome [treatment discontinuation, dose interruption or dose reduction], relationship to lenalidomide)
TFR symptoms and signs	Painful lymph nodes, painful spleen enlargement, fever[a], rash[a], lymphocytosis[a].
Other AEs	Adverse events related to lenalidomide and not listed in current EU SmPC
Death	Date and cause

AE = adverse event; eCRF = electronic case report form; EU = European Union; SmPC = Summary of Product Characteristics; TFR = tumor flare reaction.
[a] Fever, rash, or lymphocytosis alone do not constitute TFR.

A study flowchart provides additional details on the data that will be collected before and during lenalidomide treatment (Table 6).

Table 6: Study Flow Chart Showing Collection of Data Before and During Course of Lenalidomide Treatment

	Pretreatment	During Treatment
Informed Consent[a]		
Demographic Data	X	
Medical History	X	
MIPI Score	X	
Prior Stem Cell Transplantation	X	
ECOG PS	X	
Relevant Concomitant Medication	X	X
Tumor Burden Assessment	X[b]	
TFR symptoms and signs	X	X
Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC		X
Available identified laboratory data[c]	X	X

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ECOG PS = Eastern Cooperative Oncology Group Performance Status; EU = European Union; MIPI = Mantle Cell Lymphoma International Prognostic Index; PS = performance status; SmPC = Summary of Product Characteristics; TFR = tumor flare reaction.

[a] Patient informed consent, or agreement with a competent authority or another authorized third party (eg, next of kin), is to be obtained prior to data collection.

[b] Tumor burden assessment based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide.

[c] See laboratory tests in Table 3.

9.4. Data Sources

Cohort 1: Retrospective data collection from Nordic registries and national health databases

MCL patients in the Nordic countries (*inter alia*, Denmark and Sweden) will be identified through EMRs, which contain information on laboratory values, pathology/radiology results, hospital administered drugs, adverse events, and disease progression, ie, enabling identification of R/R MCL patients. The cohort identified through EMRs at chosen hospitals will then be linked to the national health registries. The national personal identity numbers assigned to each individual at birth or immigration enables linkage between various data sources, including the Cancer Registry, Patient Registry, Prescription Registry (pharmacy database), Mortality Registry. These registries contain information on demographics, patient care within in-patient and out-patient settings, comorbidities, health care resource usage, drug usage history, and cause of death. The linkage to the previously mentioned registries will be established for meeting the study objectives.

Exposure to lenalidomide will be identified through prescription registers or medical chart review, depending on dispensing pattern in the particular Nordic country.

Cohort 2: Retrospective data collection from sites

Sites where R/R MCL patients have been treated with lenalidomide will be identified in two ways via:

a) European MCL Registry

- The European MCL Registry is a multinational registry that collects medical history and treatment information on MCL patients. Sites where patients have been treated with lenalidomide for R/R MCL will be identified through the European MCL Registry. Sites are expected to participate in Germany, and in other countries where the European MCL Registry is active and where lenalidomide is reimbursed. The network will cover a population of approximately 150 million people. The European MCL Registry will identify sites with eligible patients and notify Celgene of these sites.

b) Celgene interactions with known MCL-treating sites

- Sites will also be identified by Celgene and will be approached directly once lenalidomide is reimbursed to assess the feasibility of study participation.

All sites, once identified, will be contacted to participate in the study by a contract research organization (CRO) representing Celgene. Once a site agrees to participate, the data will be collected retrospectively regarding the identified patients following the first dose of lenalidomide treatment for up to 6 months, including those patients who died within this data collection period.

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A common set of key variables (see Section 9.3) will be collected for both cohorts of the study.

9.5. Study Size

The incidence of newly diagnosed MCL (NDMCL) is 0.45 cases per 100,000 per year (Sant, 2010). With a population of 738,442,000 in Europe in 2015 (United Nations [UN] estimate), the number of NDMCL cases per year is estimated at 3,323. Of these, 67% are expected to be relapsed or refractory resulting in 2,226 R/R MCL cases per year (3,323 x 0.67).

Assuming a 10% use of lenalidomide as second-line treatment in these patients by 2018 results in an estimated 223 cases per year (2,226 x 0.10). Assuming that 60% of R/R MCL patients receive second-line treatment and that 25% of these receive third-line lenalidomide treatment by 2018 leads to an estimated 334 cases (2,226 x 0.6 x 0.25). This then gives an estimated 557 (223 + 334) cases per year of R/R MCL patients receiving second- or third-line lenalidomide treatment.

Sample size required for estimation of the cumulative incidence of TFR

Sample size calculation is based upon the observed cumulative incidence of TFR (9.6%) in the CC-5013-MCL-002 study of 167 R/R MCL patients treated with lenalidomide with an exact two-sided 95% CI = (5.6%; 15.1%). From the CC-5013-MCL-002 study, there is a 20% chance that the cumulative incidence of TFR would exceed 12.0% (upper limit of the one-sided 80% CI).

Under the assumption of a true TFR cumulative incidence rate of 9.6%, 497 patients are needed for reaching a precision of +3% on the estimate of the TFR cumulative incidence rate (upper limit of the exact two-sided 95% CI).

A sample size of 558 is required should the observed incidence of TFR reach 12% in the study population. This would give a precision of +3% based on the upper limit of the exact two-sided 95% CI. Therefore, a sample size of 560 patients will be targeted.

Estimation of early death rate

In Study CC-5013-MCL-002, 13.2% (22/167) of lenalidomide-treated patients died early. The exact two-sided 95% CI was (8.4%; 19.3%), and there is only a 20% chance that the early death rate would exceed 15.9% (upper limit of the one-sided 80% CI).

With 560 patients, the study will allow a calculation of the early death rate with a precision of +3.1% for the upper limit of the exact two-sided 95% CI if the observed rate is 13.2%, and +3.4% if it is 15.9%.

Based on market projections for lenalidomide in R/R MCL patients in Europe, the proposed study will need to accrue patients for 8 years.

9.6. Data Management

Data for the MCL PASS will be collected once patient records are complete, ie, if 6 months have elapsed after a patient received the first lenalidomide dose.

The data will be collected using an electronic case report form (eCRF).

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For each patient, data will be collected in compliance with the applicable local data protection legislation. Where applicable, the patient whose data is to be collected must date and sign the informed consent form. This information will be included on the eCRF. For patients who have died and therefore cannot provide consent and for patients recruited in the Nordic countries, local requirements for obtaining consent or consent waiver will be followed.

The data collected via an eCRF will be electronically verified through use of programmed edit checks. Discrepancies in the data will be brought to the attention of the team, and investigational site personnel, if necessary. Resolution of these issues will be reflected in the database. An audit trail within the system will track all changes made to the data. A secure electronic data collection interface licensed with the coordinating partner who will maintain its own tracking will be used for data collected from the Nordic countries.

Celgene will ensure that appropriate quality review procedures are performed during and after the study. Accuracy will be checked through programmatic edit checks according to the standard quality control procedures at the institutions conducting the data collection. For sites from the MCL network and other sites which Celgene directly contacts, the CRO will issue queries to the site for resolution. Any necessary corrections will be then applied to the data in the eCRF. If necessary, source data verification (ie, a direct comparison of the entries made in the eCRF against the patient's notes) may be conducted in a selected subgroup of sites. For the Nordic countries, a similar procedure will be followed independently by the partner responsible for the Nordic data.

9.7. Data Analysis

The analysis will be descriptive and no *a priori* hypotheses will be tested. A statistical analysis plan (SAP) will be developed for this study. All analyses will be stratified according to baseline tumor burden.

Demographic and baseline clinical characteristics will be tabulated. Dose and duration of lenalidomide and other relevant concomitant medications will be described. The proportion of patients with high tumor burden at baseline will be estimated with its two-sided 95% CI. In this study, high tumor burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.

Tumor flare reaction is an AE that presents with painful lymph nodes and/or painful spleen enlargement, and can be accompanied by fever, rash, or lymphocytosis. Early death is defined as any death occurring within 20 weeks of the initial administration of lenalidomide. The cumulative incidence of TFR and early death (both with their exact two-sided 95% CIs) will be calculated.

The frequency of TFR and other adverse events related to lenalidomide collected and not listed in the current EU Summary of Product Characteristics (SmPC) will also be reported in summary tables. Because TFR occurs early in the course of treatment, any TFR events will be descriptively reported for up to 6 months of treatment. Tumor flare reaction will be characterized by clinical assessments and laboratory tests, and tabulated by frequency, severity, seriousness, time to onset, treatment outcome (treatment discontinuation, dose interruption or dose reduction), time to resolution, and relationship to lenalidomide and tumor burden.

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Time to event analyses and incidence rates for TFR and early death will be estimated using the Kaplan-Meier (KM) method. Since data is being collected retrospectively, the number of time points each patient may have will be unknown *a priori*. Given that the precision of the KM method varies with the number of time points available for analysis and that TFR is likely to occur early in treatment with lenalidomide (time to TFR is less than 5 days for almost 25% of patients experiencing TFR and the interquartile range for time to TFR in Study MCL-002 was [0.7, 2.4] weeks [Trněný, 2016]), there will likely be an impact on the precision of the estimate using this method.

As a consequence, KM analyses will not be performed as primary but as complementary analyses.

For KM analyses, the censoring rules applying to patients for whom the event was not observed during the 6-month period following the first lenalidomide dose will be the following:

- Any patient for whom information may exist in the source database after the 6-month period following the first lenalidomide dose will be censored at 6 months.
- Any patient for whom no information exists in the source database after the 6-month period following the first lenalidomide dose will be censored at the date of the last information available in the 6-month period.

Exploration of factors associated with TFR and with early death will be conducted in multivariate analyses.

9.8. Quality Control

All data collected for the MCL PASS should be recorded accurately.

Security of the data will be maintained at all times in line with applicable local law and procedures. Access will be limited to authorized individuals. Controls, such as document encryption, will be used to ensure the authenticity, integrity, and confidentiality of electronic records when transmitted over open systems (eg, the internet). Adequate back up of the data will be maintained throughout the course of the study.

The following activities aim to ensure data quality by checking the accuracy of the data collected from medical charts, checking the completeness and validity of data in the electronic data capture (EDC) through:

- Monitoring:
  - Performing source data verification (samples rather than 100%) to ensure EDC data match source data
- Data Management:
  - Using edit checks mainly within the EDC system for more efficient data cleaning and for identification of critical missing data, required data fields, illogical, and inconsistent data

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9.9. Limitations of the Research Methods

In the design of this study, data collection will take place in different settings, and using different methods of data collection could result in missing information. To address this, a common eCRF will be used to ensure all variables and other data elements will be the same across all sources and captured in the same way. This will also facilitate in the pooling of data for analysis. Given the small size of the indication population (R/R MCL) and that patients enrolled in this study will encompass several countries across Europe, generalizability will not be a major issue.

In some countries in the Nordic region, lenalidomide is dispensed through an inpatient setting (eg, hospital pharmacies). Since hospital pharmacy data is not available through the nationwide dataset, medical chart reviews will be conducted to obtain information concerning lenalidomide exposure. In this way, Celgene can ensure a complete capture of lenalidomide exposure in the study population.

Further, AEs collected in the study that are related to lenalidomide but not listed in the current EU SmPC will be summarized and frequencies calculated. Since the study is designed with TFR as the main outcome, it may not be sufficiently powered to provide a precise estimate for these adverse reactions. However, events captured through the review of medical records will be an improvement on spontaneous reporting as these events may not have been captured through normal channels.

Although a multivariate model will be attempted to explore the relationship between TFR and early death, the sample size may not be sufficiently powered and interpretation of results should be limited to hypothesis generation. There are also limitations to the Kaplan-Meier analysis as the retrospective nature of the study and the secondary use of the data may not allow for all the information needed with appropriate time precision and correspondence with the expected time to these events.

9.10. Other Aspects

Not applicable.

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10. PROTECTION OF HUMAN SUBJECTS

Data will only be collected if the patients concerned have given their informed consent or – in cases where the patient is not able to give his/her consent – a competent authority or another authorized third party (eg, next of kin) agreed to it.

This study will complete all regulatory and ethical review requirements in accordance with applicable regulations. In addition, patients will be consented as required by the applicable regulations, including data protection legislation.

Given that this is a non-interventional study, it does not give rise to additional risks for the safety of the patients.

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11. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

This R/R MCL study is based upon secondary use of data. Reporting requirements for this non-interventional study are described in Module VI of the European Medicines Agency (EMA) Guideline on Good Pharmacovigilance Practices (GVP). Module VI (EMA, 2016) provides that "For non-interventional study designs which are based on secondary use of data, adverse reactions reporting is not required. Reports of adverse events/reactions should only be summarized in the study report, where applicable."

In addition to the information relevant to the primary objective, information on AEs related to lenalidomide and not listed in the current EU SmPC (Revlimid SmPC Section 4.8) will be collected. Common Terminology Criteria for Adverse Events (CTCAE) will be used to identify the incidence, but not the severity of the identified AEs as the study is based on retrospective data collection. The CTCAE will be used where feasible to provide a common definitional framework for the AEs collected as part of this study.

As required by the GVP modules for Periodic Safety Update Reports (PSURs) (Module VII [EMA, 2013]) and RMPs (Module V [EMA, 2016]), information on collected AEs related to lenalidomide will be included in the study report and reported appropriately in both the PSUR and the RMP. In cases of doubt, the reporting requirements will be clarified with the authorities concerned of the EU Member States.

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12. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

Regular safety updates will be made as per regulatory requirements via the PSURs. Interim analysis communications may be pursued if medical need arises.

Final data will be appropriately communicated when available, through presentation at major European or global congresses of hematology and/or oncology. Final results of the R/R MCL PASS also will be submitted for publication to an appropriate scientific and medical journal. Authorship will be based on scientific contribution to the study design and on enrollment of evaluable patients.

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ANNEX 1. LIST OF STAND-ALONE DOCUMENTS

None.

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ANNEX 2. ENCEPP CHECKLIST FOR STUDY PROTOCOLS

ENCePP Checklist for Study Protocols (Revision 2, amended)

Adopted by the ENCePP Steering Group on 14/01/2013

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) welcomes innovative designs and new methods of research. This Checklist has been developed by ENCePP to stimulate consideration of important principles when designing and writing a pharmacoepidemiological or pharmacovigilance study protocol. The Checklist is intended to promote the quality of such studies, not their uniformity. The user is also referred to the ENCePP Guide on Methodological Standards in Pharmacoepidemiology which reviews and gives direct electronic access to guidance for research in pharmacoepidemiology and pharmacovigilance.

For each question of the Checklist, the investigator should indicate whether or not it has been addressed in the study protocol. If the answer is "Yes", the page number(s) of the protocol where this issue has been discussed should be specified. It is possible that some questions do not apply to a particular study (for example in the case of an innovative study design). In this case, the answer 'N/A' (Not Applicable) can be checked and the "Comments" field included for each section should be used to explain why. The "Comments" field can also be used to elaborate on a "No" answer.

This Checklist should be included as an Annex by marketing authorization holders when submitting the protocol of a non-interventional post-authorization safety study (PASS) to a regulatory authority (see the Guidance on the format and content of the protocol of non-interventional post-authorization safety studies). Note, the Checklist is a supporting document and does not replace the format of the protocol for PASS as recommended in the Guidance and Module VIII of the Good pharmacovigilance practices (GVP).

Study title:

A Non-interventional, Post-authorization Safety Study of Patients with Relapsed or Refractory Mantle Cell Lymphoma to Further Investigate and Characterize the Association of Lenalidomide With Tumor Flare Reaction and High Tumor Burden

Study reference number:

CC-5013-MCL-005

Section 1: Milestones	**Yes**	**No**	**N/A**	**Page Number(s)**
1.1 Does the protocol specify timelines for				
1.1.1 Start of data collection[2]	☒	☐	☐	15
1.1.2 End of data collection[3]	☒	☐	☐	15
1.1.3 Study progress report(s)	☒	☐	☐	15
1.1.4 Interim progress report(s)	☒	☐	☐	15
1.1.5 Registration in the EU PAS register	☒	☐	☐	15
1.1.6 Final report of study results.	☒	☐	☐	15

Comments:

[2] Date from which information on the first study is first recorded in the study dataset or, in the case of secondary use of data, the date from which data extraction starts.
[3] Date from which the analytical dataset is completely available.

Section 2: Research question	Yes	No	N/A	Page Number(s)
2.1 Does the formulation of the research question and objectives clearly explain:				
2.1.1 Why the study is conducted? (e.g. to address an important public health concern, a risk identified in the risk management plan, an emerging safety issue)	☒	☐	☐	19
2.1.2 The objective(s) of the study?	☒	☐	☐	19
2.1.3 The target population? (i.e. population or subgroup to whom the study results are intended to be generalised)	☒	☐	☐	20-22
2.1.4 Which formal hypothesis(-es) is (are) to be tested?	☐	☐	☒	
2.1.5 If applicable, that there is no *a priori* hypothesis?	☒	☐	☐	27

Comments:

Section 3: Study design	Yes	No	N/A	Page Number(s)
3.1 Is the study design described? (e.g. cohort, case-control, randomised controlled trial, new or alternative design)	☒	☐	☐	20-22
3.2 Does the protocol specify the primary and secondary (if applicable) endpoint(s) to be investigated?	☒	☐	☐	19
3.3 Does the protocol describe the measure(s) of effect? (e.g. relative risk, odds ratio, deaths per 1000 person-years, absolute risk, excess risk, incidence rate ratio, hazard ratio, number needed to harm (NNH) per year)	☐	☒	☐	

Comments:

Section 4: Source and study populations	Yes	No	N/A	Page Number(s)
4.1 Is the source population described?	☒	☐	☐	25-26
4.2 Is the planned study population defined in terms of:				
4.2.1 Study time period?	☒	☐	☐	21
4.2.2 Age and sex?	☒	☐	☐	21
4.2.3 Country of origin?	☒	☐	☐	25-26
4.2.4 Disease/indication?	☒	☐	☐	19-25
4.2.5 Co-morbidity?	☐	☒	☐	
4.2.6 Seasonality?	☐	☒	☐	

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Section 4: Source and study populations	**Yes**	**No**	**N/A**	**Page Number(s)**
4.3 Does the protocol define how the study population will be sampled from the source population? (e.g. event or inclusion/exclusion criteria)	☒	☐	☐	21

Comments:

Section 5: Exposure definition and measurement	**Yes**	**No**	**N/A**	**Page Number(s)**
5.1 Does the protocol describe how exposure is defined and measured? (e.g. operational details for defining and categorising exposure)	☒	☐	☐	21
5.2 Does the protocol discuss the validity of exposure measurement? (e.g. precision, accuracy, prospective ascertainment, exposure information recorded before the outcome occurred, use of validation sub-study)	☒	☐	☐	21
5.3 Is exposure classified according to time windows? (e.g. current user, former user, non-use)	☒	☐	☐	21
5.4 Is exposure classified based on biological mechanism of action and taking into account the pharmacokinetics and pharmacodynamics of the drug?	☐	☐	☒	
5.5 Does the protocol specify whether a dose-dependent or duration-dependent response is measured?	☐	☐	☒	

Comments:

Section 6: Endpoint definition and measurement	**Yes**	**No**	**N/A**	**Page Number(s)**
6.1 Does the protocol describe how the endpoints are defined and measured?	☒	☐	☐	27-28
6.2 Does the protocol discuss the validity of endpoint measurement? (e.g. precision, accuracy, sensitivity, specificity, positive predictive value, prospective or retrospective ascertainment, use of validation sub-study)	☒	☐	☐	27-28

Comments:

Section 7: Confounders and effect modifiers	**Yes**	**No**	**N/A**	**Page Number(s)**
7.1 Does the protocol address known confounders? (e.g. collection of data on known confounders, methods of controlling for known confounders)	☐	☒	☐	

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Section 7: Confounders and effect modifiers	**Yes**	**No**	**N/A**	**Page Number(s)**
7.2 Does the protocol address known effect modifiers? (e.g. collection of data on known effect modifiers, anticipated direction of effect)	☐	☒	☐	

Comments:

Section 8: Data sources	**Yes**	**No**	**N/A**	**Page Number(s)**
8.1 Does the protocol describe the data source(s) used in the study for the ascertainment of:				
8.1.1 Exposure? (e.g. pharmacy dispensing, general practice prescribing, claims data, self-report, face-to-face interview, etc.)	☒	☐	☐	25-26
8.1.2 Endpoints? (e.g. clinical records, laboratory markers or values, claims data, self-report, patient interview including scales and questionnaires, vital statistics, etc.)	☒	☐	☐	25-26
8.1.3 Covariates?	☒	☐	☐	25-26
8.2 Does the protocol describe the information available from the data source(s) on:				
8.2.1 Exposure? (e.g. date of dispensing, drug quantity, dose, number of days of supply prescription, daily dosage, prescriber)	☒	☐	☐	25-26
8.2.2 Endpoints? (e.g. date of occurrence, multiple event, severity measures related to event)	☒	☐	☐	25-26
8.2.3 Covariates? (e.g. age, sex, clinical and drug use history, co-morbidity, co-medications, life style, etc.)	☒	☐	☐	25-26
8.3 Is a coding system described for:				
8.3.1 Diseases? (e.g. International Classification of Diseases (ICD)-10)	☐	☒	☐	
8.3.2 Endpoints? (e.g. Medical Dictionary for Regulatory Activities (MedDRA) for adverse events)	☒	☐	☐	31
8.3.3 Exposure? (e.g. WHO Drug Dictionary, Anatomical Therapeutic Chemical (ATC)Classification System)	☐	☐	☒	
8.4 Is the linkage method between data sources described? (e.g. based on a unique identifier or other)	☒	☐	☐	25

Comments:

Section 9: Study size and power	**Yes**	**No**	**N/A**	**Page Number(s)**
9.1 Is sample size and/or statistical power calculated?	☒	☐	☐	26-28

Comments:

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Section 10: Analysis plan	**Yes**	**No**	**N/A**	**Page Number(s)**
10.1 Does the plan include measurement of excess risks?	☐	☐	☒	
10.2 Is the choice of statistical techniques described?	☒	☐	☐	27-28
10.3 Are descriptive analyses included?	☒	☐	☐	27-28
10.4 Are stratified analyses included?	☒	☐	☐	27-28
10.5 Does the plan describe methods for adjusting for confounding?	☐	☐	☒	
10.6 Does the plan describe methods addressing effect modification?	☐	☐	☒	

Comments:

Section 11: Data management and quality control	**Yes**	**No**	**N/A**	**Page Number(s)**
11.1 Is information provided on the management of missing data?	☒	☐	☐	28-29
11.2 Does the protocol provide information on data storage? (e.g. software and IT environment, database maintenance and anti-fraud protection, archiving)	☒	☐	☐	28
11.3 Are methods of quality assurance described?	☒	☐	☐	28
11.4 Does the protocol describe possible quality issues related to the data source(s)?	☒	☐	☐	29
11.5 Is there a system in place for independent review of study results?	☐	☐	☒	

Comments:

Section 12: Limitations	**Yes**	**No**	**N/A**	**Page Number(s)**
12.1 Does the protocol discuss:				
12.1.1 Selection biases?	☒	☐	☐	28-29
12.1.2 Information biases? (e.g. anticipated direction and magnitude of such biases, validation sub-study, use of validation and external data, analytical methods)	☒	☐	☐	28-29
12.2 Does the protocol discuss study feasibility? (e.g. sample size, anticipated exposure, duration of follow-up in a cohort study, patient recruitment)	☒	☐	☐	28-29
12.3 Does the protocol address other limitations?	☒	☐	☐	28-29

Comments:

Section 13: Ethical issues	Yes	No	N/A	Page Number(s)
13.1 Have requirements of Ethics Committee/Institutional Review Board approval been described?	☒	☐	☐	30
13.2 Has any outcome of an ethical review procedure been addressed?	☐	☐	☒	
13.3 Have data protection requirements been described?	☒	☐	☐	26-27

Comments:

Section 14: Amendments and deviations	Yes	No	N/A	Page Number(s)
14.1 Does the protocol include a section to document future amendments and deviations?	☒	☐	☐	14

Comments:

Section 15: Plans for communication of study results	Yes	No	N/A	Page Number(s)
15.1 Are plans described for communicating study results (e.g. to regulatory authorities)?	☒	☐	☐	32
15.2 Are plans described for disseminating study results externally, including publication?	☒	☐	☐	32

Comments:

Name of the main authors of the protocol: [redacted]

Date: 19 Jul 2017

Signature: [redacted]

Date: 19 Jul 2017

Signature: [redacted]

Approved v1.0 930231036 1.0

EDMS Doc. Number: 22019562 - 21272015

ANNEX 3. ADDITIONAL INFORMATION

Not applicable.

Approved v1.0 930231036 1.0

EDMS Doc. Number: 22019562 - 21272015

Celgene Signing Page

This is a representation of an electronic record that was signed electronically in Livelink. This page is the manifestation of the electronic signature(s) used in compliance with the organizations electronic signature policies and procedures.

UserName: [redacted]
Title: Exec.Dir. Glob.Safety EEA QPPV
Date: Monday, 07 August 2017, 07:24 AM Eastern Daylight Time
Meaning: Approved, no changes necessary.
==========

UserName: [redacted]
Title: VP, Med Aff, Hem/Onc EMEA
Date: Monday, 07 August 2017, 04:06 PM Eastern Daylight Time
Meaning: Approved, no changes necessary.
==========

APPENDIX 1.2 Sample Case Report Form

120 page(s) excluding cover page

Approved v1.0 930231036 1.0

APPENDIX 1.2 Sample Case Report Form

- Case Report Form

Subject ID _____ 1

0008 CC-5013-MCL-005_CPPC2: UNIQUE
Project Name: CC-5013-MCL-005
Form: Subject
Generated On: 23 Oct 2020 11:54:19

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	SUBJID	$7			

What is the visit date? _____ 1

0008 CC-5013-MCL-005_CPPC2: UNIQUE
Project Name: CC-5013-MCL-005
Form: Date of Visit
Generated On: 23 Oct 2020 11:54:19

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	M_VISDAT	dd-/MMM-/yyyy			

0008 CC-5013-MCL-005_CPPC2: UNIQUE
Project Name: CC-5013-MCL-005
Form: Demographics
Generated On: 23 Oct 2020 11:54:19

What is the subject's date of birth?	_____	1
Derived Age	_____	2
Derived Age Unit	YEARS ☐	3
Enter age at time of informed consent	_____	4
Age Unit	YEARS ■	5
What is the sex of the subject?	Female ☐ Male ☐	6
What is the primary race of the subject?	AMERICAN INDIAN OR ALASKA NATIVE ☐ ASIAN ☐ BLACK OR AFRICAN AMERICAN ☐ NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER ☐ WHITE ☐ NOT COLLECTED OR REPORTED ■ OTHER ☐	7

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	M_BRTHDAT	dd-/MMM-/yyyy			
2	DV_AGE	3			
3	DV_AGEU	$10		C29848 = YEARS	
4	AGE	3			
5	AGEU	$10		C29848 = YEARS	
6	M_SEX	$10		1 = Female 2 = Male	
7	RACE	$10		C41259 = AMERICAN INDIAN OR ALASKA NATIVE C41260 = ASIAN C16352 = BLACK OR AFRICAN AMERICAN C41219 = NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C41261 = WHITE 996 = NOT COLLECTED OR REPORTED C17649 = OTHER	

Protocol Version 3 – original version provided to sites

Protocol Version 4 – First protocol amendment provided to sites.

What type of informed consent was obtained?	INFORMED CONSENT OBTAINED ☐ 2
Was consent obtained for the indicated consent type?	Yes ☐ 3 No ☐ Not Applicable ☐
If Not Applicable, please specify	LEGAL EXEMPTION FOR INFORMED CONSENT ☐ 4 AUTHORIZATION BY COMPETENT AUTHORITIES ☐ AUTHORIZATION BY AUTHORIZED THIRD PERSON ☐
What was the date the informed consent was obtained?	_____ 5
If the subject signed informed consent for a new protocol amendment, indicate the amendment number.	PROTOCOL AMENDMENT 1 ☐ 6 PROTOCOL AMENDMENT 2 ☐ PROTOCOL AMENDMENT 3 ☐ PROTOCOL AMENDMENT 4 ☐ PROTOCOL AMENDMENT 5 ☐ PROTOCOL AMENDMENT 6 ☐ PROTOCOL AMENDMENT 7 ☐ PROTOCOL AMENDMENT 8 ☐ PROTOCOL AMENDMENT 9 ☐ PROTOCOL AMENDMENT 10 ☐

	Field Name	Data Type	Units	Values	Pre-Filled Values
2	M_DSTERM_3IC			710 = INFORMED CONSENT OBTAINED	1: INFORMED CONSENT OBTAINED
3	X_DSICYN	$10		C49488 = Yes C49487 = No C48660 = Not Applicable	
4	M_DSTERM_$10ICOTH			X0604001 = LEGAL EXEMPTION FOR INFORMED CONSENT X0604003 = AUTHORIZATION BY COMPETENT AUTHORITIES X0604002 = AUTHORIZATION BY AUTHORIZED THIRD PERSON	
5	M_DSSTDAT	dd-/MMM-/yyyy			
6	M_QVAL_PR3OTVER			1 = PROTOCOL AMENDMENT 1	

Field Name	Data Type	Units	Values	Pre-Filled Values
			2 = PROTOCOL AMENDMENT 2 3 = PROTOCOL AMENDMENT 3 4 = PROTOCOL AMENDMENT 4 5 = PROTOCOL AMENDMENT 5 6 = PROTOCOL AMENDMENT 6 7 = PROTOCOL AMENDMENT 7 8 = PROTOCOL AMENDMENT 8 9 = PROTOCOL AMENDMENT 9 10 = PROTOCOL AMENDMENT 10	

Protocol Version 3 – original version provided to sites

Protocol Version 4 – First protocol amendment provided to sites.

What is the version of the protocol under which the subject enrolled?

- VERSION 3.0 ☐ 2
- VERSION 4.0 ☐
- VERSION 5.0 ☐
- VERSION 6.0 ☐
- VERSION 7.0 ☐
- VERSION 8.0 ☐
- VERSION 9.0 ☐
- VERSION 10.0 ☐

Did the subject meet all eligibility criteria?

- Yes ☐ 3
- No ☐

If No, enter the Inclusion and Exclusion criteria for which the subject failed

What was the category of the criterion?

- EXCLUSION ☐ 5
- INCLUSION ☐

What is the ID of the criterion the subject did not meet?

- Exclusion 1 ☐ 6
- Inclusion 1 ☐
- Inclusion 2 ☐
- Inclusion 3 ☐

	Field Name	Data Type	Units	Values	Pre-Filled Values
2	M_IEPROTV	3		13 = VERSION 3.0 14 = VERSION 4.0 15 = VERSION 5.0 16 = VERSION 6.0 17 = VERSION 7.0 18 = VERSION 8.0 19 = VERSION 9.0 20 = VERSION 10.0	
3	X_IEYN	$10		C49488 = Yes C49487 = No	
5	IECAT	$10		C25370 = EXCLUSION C25532 = INCLUSION	
6	M_IETESTC	$5		E1 = Exclusion 1 I1 = Inclusion 1 I2 = Inclusion 2 I3 = Inclusion 3	

What is the date of the subject's death? ① _____

What was the reported primary cause of death? ② _____

or

Check if primary cause of death is unknown Unknown ☐ ④

Reported Term for the Disposition Event, if unknown ⑤ _____

0008 CC-5013-MCL-005_CPPC2: UNIQUE
Project Name: CC-5013-MCL-005
Form: Death
Generated On: 23 Oct 2020 11:54:19

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	M_DSSTDAT	dd-/MMM-/yyyy			
2	M_DSTERM_DTH	$200			
4	M_DDORRES_UNDTH	$10		C17998 = Unknown	
5	DV_DDORRES_UNDTH	$200			

Trial period for which the Status is being Reported (1)

- BLINDED TREATMENT ☐
- CONTINUATION TREATMENT ☐
- FOLLOW-UP ☐
- INDUCTION TREATMENT ☐
- LONG-TERM FOLLOW-UP ☐
- OPEN LABEL TREATMENT ☐
- RUN-IN ☐
- SCREENING ☐
- TREATMENT ☐
- WASHOUT ☐
- SCREENING-STANDARD OF CARE ☐
- TREATMENT-STANDARD OF CARE ☐
- PRE-TREATMENT EVALUATION ☐
- RETREATMENT EVALUATION ☐
- PRE-TREATMENT ☐
- STUDY DISCONTINUATION ■
- END OF STUDY ☐

Date of Completion/Discontinuation (2) _____

What was the subject's status at study discontinuation? (3)

- COMPLETED ☐
- DEATH ☐
- LOST TO FOLLOW-UP ☐
- WITHDRAWAL BY SUBJECT ☐
- PARTICIPATING IN AN INTERVENTIONAL CLINICAL TRIAL ☐
- SCREEN FAILURE ☐

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	EPOCH	$10		C102255 = BLINDED TREATMENT C123452 = CONTINUATION TREATMENT C99158 = FOLLOW-UP C123453 = INDUCTION TREATMENT C16032 = LONG-TERM FOLLOW-UP C102256 = OPEN LABEL TREATMENT C98779 = RUN-IN C48262 = SCREENING C101526 = TREATMENT C42872 = WASHOUT X99079001 = SCREENING-STANDARD OF CARE X99079002 = TREATMENT-STANDARD OF CARE	

	Field Name	Data Type	Units	Values	Pre-Filled Values
				X99079003 = PRE-TREATMENT EVALUATION X99079004 = RETREATMENT EVALUATION X99079005 = PRE-TREATMENT X99079006 = STUDY DISCONTINUATION X99079007 = END OF STUDY	
2	M_DSSTDAT	dd-/MMM-/yyyy			
3	M_DSTERM	$10		C25250 = COMPLETED C28554 = DEATH C48227 = LOST TO FOLLOW-UP C49634 = WITHDRAWAL BY SUBJECT	

Field Name	Data Type	Units	Values	Pre-Filled Values
			S001 = PARTICIPATING IN AN INTERVENTIONAL CLINICAL TRIAL C49628 = SCREEN FAILURE	

Prior History — TUMOR FLARE REACTION (1)

Did the History Occur? — Yes ☐ (2) / No ☐

If yes, reason why subject was treated with Lenalidomide _____ (3)

What was the date the medical history event or condition started or was diagnosed? _____ (4)

Check if the start date is unknown _____ (5)

Is the medical history disease/condition or event still ongoing? — Yes ☐ (6) / No ☐

If no, what was the date the medical history event or condition ended? _____ (7)

Check if the end date is unknown _____ (8)

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	MHTERM_PRIOR	$10		Y0178005 = TUMOR FLARE REACTION	
2	M_MHOCCUR_MHSTAT	$10		C49488 = Yes C49487 = No	
3	M_QVAL_REASTRT	$200			
4	M_MHSTDAT	dd-/MMM-/yyyy			
5	X_MHSTDATUN	1			
6	M_MHONGO	$10		C49488 = Yes C49487 = No	
7	M_MHENDAT	dd-/MMM-/yyyy			
8	X_MHENDATUN	1			

Does the subject have any medical history to report? Yes ☐ No ☐ (1)

What is the verbatim term for the medical history condition/event? _____ (2)

What was the date the medical history event or condition started or was diagnosed? _____ (3)

Check if the start date is unknown _____ (4)

Is the medical history disease/condition or event still ongoing? Yes ☐ No ☐ (5)

If no, what was the date the medical history event or condition ended? _____ (6)

Check if the end date is unknown _____ (7)

0008 CC-5013-MCL-005_CPPC2: UNIQUE
Project Name: CC-5013-MCL-005
Form: Medical History
Generated On: 23 Oct 2020 11:54:19

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	X_MHYN	$10		C49488 = Yes C49487 = No	
2	MHTERM	$200			
3	M_MHSTDAT	dd-/MMM-/yyyy			
4	X_MHSTDATUN	1			
5	M_MHONGO	$10		C49488 = Yes C49487 = No	
6	M_MHENDAT	dd-/MMM-/yyyy			
7	X_MHENDATUN	1			

Was the sample collected?	Yes ☐ 1 No ☐
What was the specimen collection date?	_____ 2
Sodium, Serum/Plasma	NOT DONE ☐ 3
Potassium, Serum/Plasma	NOT DONE ☐ 4
Calcium, Serum/Plasma	NOT DONE ☐ 5
Phosphate, Serum/Plasma	NOT DONE ☐ 6
Creatinine, Serum/Plasma	NOT DONE ☐ 7
Creatinine Clearance, Cockcroft-Gault Serum/Plasma	NOT DONE ☐ 8
Estimated Glomerular Filtration Rate Adj for BSA (MDRD), Serum/Plasma	NOT DONE ☐ 9
Estimated Glomerular Filtration Rate Adj for BSA (CKD-EPI), Serum/Plasma	NOT DONE ☐ 10
Glucose, Serum/Plasma Random	NOT DONE ☐ 11
Lactate Dehydrogenase (LDH), Serum/Plasma	NOT DONE ☐ 12
Alanine Aminotransferase (ALT), Serum/Plasma	NOT DONE ☐ 13

Aspartate Aminotransferase (AST), Serum/Plasma	NOT DONE ☐	14
Total Bilirubin, Serum/Plasma	NOT DONE ☐	15
Direct Bilirubin, Serum/Plasma	NOT DONE ☐	16
Albumin, Serum/Plasma	NOT DONE ☐	17
C Reactive Protein (CRP), Serum/Plasma	NOT DONE ☐	18
Sodium, Serum/Plasma		19
Potassium, Serum/Plasma		20
Calcium, Serum/Plasma		21
Phosphate, Serum/Plasma		22
Creatinine, Serum/Plasma		23
Creatinine Clearance, Cockcroft-Gault Serum/Plasma		24
Estimated Glomerular Filtration Rate Adj for BSA (MDRD), Serum/Plasma		25
Estimated Glomerular Filtration Rate Adj for BSA (CKD-EPI), Serum/Plasma		26
Glucose, Serum/Plasma Random		27

Lactate Dehydrogenase (LDH), Serum/Plasma	28
Alanine Aminotransferase (ALT), Serum/Plasma	29
Aspartate Aminotransferase (AST), Serum/Plasma	30
Total Bilirubin, Serum/Plasma	31
Direct Bilirubin, Serum/Plasma	32
Albumin, Serum/Plasma	33
C Reactive Protein (CRP), Serum/Plasma	34

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	M_LBPERF	$10		C49488 = Yes C49487 = No	
2	M_LBDAT	dd-/MMM-/yyyy			
3	M_LBSTAT_SODIUM_SERPLAS	$10		C49484 = NOT DONE	
4	M_LBSTAT_K_SERPLAS	$10		C49484 = NOT DONE	
5	M_LBSTAT_CA_SERPLAS	$10		C49484 = NOT DONE	
6	M_LBSTAT_PHOS_SERPLAS	$10		C49484 = NOT DONE	
7	M_LBSTAT_CREAT_SERPLAS	$10		C49484 = NOT DONE	
8	M_LBSTAT_CREATCLR_SERPLAS	$10		C49484 = NOT DONE	
9	M_LBSTAT_GFRE_SERPLAS	$10		C49484 = NOT DONE	

	Field Name	Data Type	Units	Values	Pre-Filled Values
10	M_LBSTAT_GFRBSCRT_SERPLA_CKDEPI	$10		C49484 = NOT DONE	
11	M_LBSTAT_GLUC_SERPLAS_RANDOM	$10		C49484 = NOT DONE	
12	M_LBSTAT_LDH_SERPLAS	$10		C49484 = NOT DONE	
13	M_LBSTAT_ALT_SERPLAS	$10		C49484 = NOT DONE	
14	M_LBSTAT_AST_SERPLAS	$10		C49484 = NOT DONE	
15	M_LBSTAT_BILI_SERPLAS	$10		C49484 = NOT DONE	
16	M_LBSTAT_BILDIR_SERPLAS	$10		C49484 = NOT DONE	
17	M_LBSTAT_ALB_SERPLAS	$10		C49484 = NOT DONE	

	Field Name	Data Type	Units	Values	Pre-Filled Values
18	M_LBSTAT_CRP_SERPLAS	$10		C49484 = NOT DONE	
19	M_LBORRES_SODIUM_SERPLAS	16.7			
20	M_LBORRES_K_SERPLAS	16.7			
21	M_LBORRES_CA_SERPLAS	16.7			
22	M_LBORRES_PHOS_SERPLAS	16.7			
23	M_LBORRES_CREAT_SERPLAS	16.7			
24	M_LBORRES_CREATCLR_SERPLAS	16.7			
25	M_LBORRES_GFRE_SERPLAS	16.7			

	Field Name	Data Type	Units	Values	Pre-Filled Values
26	M_LBORRES_GFRBSCRT_SERPLA_CKDEPI	16.7			
27	M_LBORRES_GLUC_SERPLAS_RANDOM	16.7			
28	M_LBORRES_LDH_SERPLAS	16.7			
29	M_LBORRES_ALT_SERPLAS	16.7			
30	M_LBORRES_AST_SERPLAS	16.7			
31	M_LBORRES_BILI_SERPLAS	16.7			
32	M_LBORRES_BILDIR_SERPLAS	16.7			
33	M_LBORRES_ALB_SERPLAS	16.7			

	Field Name	Data Type	Units	Values	Pre-Filled Values
34	M_LBORRES_CRP_SERPLAS	16.7			

Was the sample collected?	Yes ☐ 1 No ☐
What was the specimen collection date?	_____ 2
Hemoglobin (HGB), Blood	NOT DONE ☐ 3
Platelets (Thrombocytes)	NOT DONE ☐ 4
Leukocytes (WBC), Blood	NOT DONE ☐ 5
Absolute Lymphocytes	NOT DONE ☐ 6
Absolute Neutrophils (ANC)	NOT DONE ☐ 7
Circulating Tumor Cells, Blood	NOT DONE ☐ 8
Hemoglobin (HGB), Blood	_____ 9
Platelets (Thrombocytes)	_____ 10
Leukocytes (WBC), Blood	_____ 11
Absolute Lymphocytes	_____ 12
Absolute Neutrophils (ANC)	_____ 13
Circulating Tumor Cells, Blood	_____ 14

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	M_LBPERF	$10		C49488 = Yes C49487 = No	
2	M_LBDAT	dd-/MMM-/yyyy			
3	M_LBSTAT_HGB_BLOOD	$10		C49484 = NOT DONE	
4	M_LBSTAT_PLAT	$10		C49484 = NOT DONE	
5	M_LBSTAT_WBC_BLOOD	$10		C49484 = NOT DONE	
6	M_LBSTAT_LYM	$10		C49484 = NOT DONE	
7	M_LBSTAT_NEUT	$10		C49484 = NOT DONE	
8	M_LBSTAT_CTC_BLOOD	$10		C49484 = NOT DONE	
9	M_LBORRES_HGB_BLOOD	16.7			

	Field Name	Data Type	Units	Values	Pre-Filled Values
10	M_LBORRES_PLAT	16.7			
11	M_LBORRES_WBC_BLOOD	16.7			
12	M_LBORRES_LYM	16.7			
13	M_LBORRES_NEUT	16.7			
14	M_LBORRES_CTC_BLOOD	16.7			

Was the assessment performed? Yes ☐ 1 No ☐

Date of Assessment _____ 2

What was the grade of the assessment? 0 ☐ 3
1 ☐
2 ☐
3 ☐
4 ☐

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	M_QSPERF	$10		C49488 = Yes C49487 = No	
2	M_QSDAT	dd-/MMM-/yyyy			
3	M_QSORRES_ECOG	3		0 = 0 1 = 1 2 = 2 3 = 3 4 = 4	

Were there any Adverse Events? Yes ☐ 1 No ☐

Were any Concomitant Medications taken? Yes ☐ 2 No ☐

Were there any Prior/Concomitant Procedures/Surgeries? Yes ☐ 3 No ☐

0008 CC-5013-MCL-005_CPPC2: UNIQUE
Project Name: CC-5013-MCL-005
Form: Prompt- AE CONMED and PROC
Generated On: 23 Oct 2020 11:54:19

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	X_AEYN	$10		C49488 = Yes C49487 = No	
2	X_CMYN	$10		C49488 = Yes C49487 = No	
3	X_PRYN	$10		C49488 = Yes C49487 = No	

What is the adverse event term? _____ 1

Category for adverse event
- TUMOR FLARE REACTION ☐ 2
- OTHER ☐

What is the date the adverse event started? _____ 3

Is the adverse event still ongoing?
- Yes ☐ 4

What date did the adverse event end? _____ 5

What is the toxicity grade of the adverse event? 6
- 1 ☐
- 2 ☐
- 3 ☐
- 4 ☐
- 5 ☐

Is the adverse event serious? 7
- Yes ☐
- No ☐

Is this event related to study treatment? 8
- SUSPECTED ☐
- NOT SUSPECTED ☐

What action was taken with study treatment? 9
- DOSE NOT CHANGED ☐
- DOSE REDUCED ☐
- DRUG INTERRUPTED ☐
- DRUG WITHDRAWN ☐
- DOSE INCREASED ☐
- NOT APPLICABLE ☐

What was the outcome of this adverse event?

- FATAL ☐ 10
- NOT RECOVERED/NOT RESOLVED ☐
- RECOVERED/RESOLVED ☐
- RECOVERED/RESOLVED WITH SEQUELAE ☐
- UNKNOWN ☐

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	AETERM	$200			
2	AECAT	3		212 = TUMOR FLARE REACTION 211 = OTHER	
3	M_AESTDAT	dd-/MMM-/yyyy			
4	M_AEONGO	$10		C49488 = Yes	
5	M_AEENDAT	dd-/MMM-/yyyy			
6	AETOXGR	$10		C84263 = 1 C84264 = 2 C84265 = 3 C84266 = 4 C48275 = 5	
7	AESER	$10		C49488 = Yes C49487 = No	
8	AEREL	3		1 = SUSPECTED 2 = NOT SUSPECTED	

	Field Name	Data Type	Units	Values	Pre-Filled Values
9	AEACN	$10		C49504 = DOSE NOT CHANGED C49505 = DOSE REDUCED C49501 = DRUG INTERRUPTED C49502 = DRUG WITHDRAWN C49503 = DOSE INCREASED C48660 = NOT APPLICABLE	
10	AEOUT	$10		C48275 = FATAL C49494 = NOT RECOVERED/NOT RESOLVED C49498 = RECOVERED/RESOLVED C49495 = RECOVERED/RESOLVED WITH SEQUELAE	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C17998 = UNKNOWN	

What was the term for the medication taken? _____ (1)

Category for Medication (2)
- ☐ MCL TREATMENT LINE - STANDARD CARE
- ☐ GENERAL

What was the **primary** reason the medication was taken? (3)
- ☐ ADVERSE EVENT
- ☐ MEDICAL HISTORY
- ☐ OTHER

If the primary reason for the medication is AE or MH, select the ID of the primary event. _____ (4)

If the primary reason for the medication is **other** than AE or MH, enter the primary term of the indication. _____ (5)

If there are additional AEs that are indications for this medication, enter the AE ID separated by semicolons (;) _____ (6)

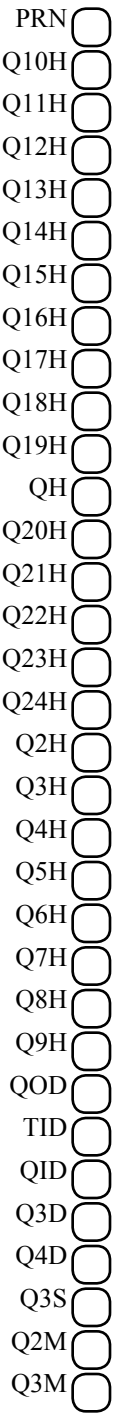
If there are additional MH events that are indications for this medication, enter the MH ID separated by semicolons (;) _____ (7)

If there are additional indications for this medication that are not AEs or MH, enter the indications separated by semicolons (;) _____ (8)

What was the individual dose of the medication/therapy? _____ (9)

What was the unit of the medication/therapy? _____ (10)

What was the frequency of the medication/therapy? (11)
- ☐ CONTINUOUS
- ☐ BID
- ☐ QM


PRN
Q10H
Q11H
Q12H
Q13H
Q14H
Q15H
Q16H
Q17H
Q18H
Q19H
QH
Q20H
Q21H
Q22H
Q23H
Q24H
Q2H
Q3H
Q4H
Q5H
Q6H
Q7H
Q8H
Q9H
QOD
TID
QID
Q3D
Q4D
Q3S
Q2M
Q3M

Q4M
ONCE
Q5D
BIM
INTERMITTENT
QD
OCCASIONAL
AD LIBITUM
1 TIME PER WEEK
2 TIMES PER YEAR
3 TIMES PER MONTH
3 TIMES PER YEAR
4 TIMES PER MONTH
4 TIMES PER YEAR
5 TIMES PER DAY
5 TIMES PER MONTH
5 TIMES PER WEEK
5 TIMES PER YEAR
6 TIMES PER DAY
6 TIMES PER MONTH
6 TIMES PER WEEK
6 TIMES PER YEAR
7 TIMES PER WEEK
PA
Q6S
UNKNOWN
EVERY WEEK
EVERY 2 WEEKS
EVERY 4 WEEKS
QAM
QPM
2 TIMES PER WEEK
3 TIMES PER WEEK

4 TIMES PER WEEK ☐

What was the route of administration of the medication/therapy?

AURICULAR (OTIC) ☐ 12
BUCCAL ☐
CONJUNCTIVAL ☐
CUTANEOUS ☐
DENTAL ☐
ELECTRO-OSMOSIS ☐
ENDOCERVICAL ☐
ENDOSINUSIAL ☐
ENDOTRACHEAL ☐
ENTERAL ☐
EPIDURAL ☐
EXTRA-AMNIOTIC ☐
EXTRACORPOREAL ☐
HEMODIALYSIS ☐
INFILTRATION ☐
INTERSTITIAL ☐
INTRA-ABDOMINAL ☐
INTRA-AMNIOTIC ☐
INTRA-ARTERIAL ☐
INTRA-ARTICULAR ☐
INTRABILIARY ☐
INTRABRONCHIAL ☐
INTRABURSAL ☐
INTRACARDIAC ☐
INTRACARTILAGINOUS ☐
INTRACAUDAL ☐
INTRACAVERNOUS ☐
INTRACAVITARY ☐
INTRACEREBRAL ☐
INTRACISTERNAL ☐
INTRACORNEAL ☐

INTRACORONAL, DENTAL ☐
INTRACORONARY ☐
INTRACORPORUS CAVERNOSUM ☐
INTRADERMAL ☐
INTRADISCAL ☐
INTRADUCTAL ☐
INTRADUODENAL ☐
INTRADURAL ☐
INTRAEPIDERMAL ☐
INTRAESOPHAGEAL ☐
INTRAGASTRIC ☐
INTRAGINGIVAL ☐
INTRAILEAL ☐
INTRALESIONAL ☐
INTRALUMINAL ☐
INTRALYMPHATIC ☐
INTRAMEDULLARY ☐
INTRAMENINGEAL ☐
INTRAMUSCULAR ☐
INTRAOCULAR ☐
INTRAOVARIAN ☐
INTRAPERICARDIAL ☐
INTRAPERITONEAL ☐
INTRAPLEURAL ☐
INTRAPROSTATIC ☐
INTRAPULMONARY ☐
INTRASINAL ☐
INTRASPINAL ☐
INTRASYNOVIAL ☐
INTRATENDINOUS ☐
INTRATESTICULAR ☐
INTRATHECAL ☐

- [ ] INTRATHORACIC
- [ ] INTRATUBULAR
- [ ] INTRATUMOR
- [ ] INTRATYMPANIC
- [ ] INTRAUTERINE
- [ ] INTRAVASCULAR
- [ ] INTRAVENOUS
- [ ] INTRAVENOUS BOLUS
- [ ] INTRAVENOUS DRIP
- [ ] INTRAVENTRICULAR
- [ ] INTRAVESICAL
- [ ] INTRAVITREAL
- [ ] IONTOPHORESIS
- [ ] IRRIGATION
- [ ] LARYNGEAL
- [ ] NASAL
- [ ] NASOGASTRIC
- [ ] NOT APPLICABLE
- [ ] OCCLUSIVE DRESSING TECHNIQUE
- [ ] OPHTHALMIC
- [ ] ORAL
- [ ] OROPHARYNGEAL
- [ ] PARENTERAL
- [ ] PERCUTANEOUS
- [ ] PERIARTICULAR
- [ ] PERIDURAL
- [ ] PERINEURAL
- [ ] PERIODONTAL
- [ ] RECTAL
- [ ] RESPIRATORY (INHALATION)
- [ ] RETROBULBAR
- [ ] SOFT TISSUE

SUBARACHNOID ☐
SUBCONJUNCTIVAL ☐
SUBCUTANEOUS ☐
SUBLINGUAL ☐
SUBMUCOSAL ☐
TOPICAL ☐
TRANSDERMAL ☐
TRANSMUCOSAL ☐
TRANSPLACENTAL ☐
TRANSTRACHEAL ☐
TRANSTYMPANIC ☐
UNASSIGNED ☐
URETERAL ☐
URETHRAL ☐
VAGINAL ☐
DIETARY ☐
ORAL GAVAGE ☐
INTRASTOMAL ☐
INTRAJEJUNAL ☐
INTRAPALATAL ☐
UNKNOWN ☐
OTHER ☐

If Other Route, Specify _____ 13

What was the start date of the medication/therapy? _____ 14

Check if the date is unknown _____ 15

If unknown, did the medication start before the first dose of study treatment? Yes ☐ 16 No ☐

Is the medication/therapy still ongoing at the time of disposition? Yes ☐ No ☐ 17

What was the end date of the medication/therapy? _____ 18

Check if the end date is unknown _____ 19

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	CMTRT	$200			
2	CMCAT	$10		Y0145021 = MCL TREATMENT LINE - STANDARD CARE X0145009 = GENERAL	
3	X_CMINDCAT	$10		1 = ADVERSE EVENT 2 = MEDICAL HISTORY C17649 = OTHER	
4	M_CMINDC_AEMH	$120			
5	M_CMINDC_OTH	$200			
6	M_IDVARVAL_AESPID	$40			
7	M_IDVARVAL_MHSPID	$40			
8	M_QVAL_CMINDCO	$200			

	Field Name	Data Type	Units	Values	Pre-Filled Values
9	M_CMDSTXT	$200			
10	CMDOSU	$10		UNIT	
11	CMDOSFRQ	$10		C53279 = CONTINUOUS C64496 = BID C64498 = QM C64499 = PRN C64500 = Q10H C64501 = Q11H C64502 = Q12H C64503 = Q13H C64504 = Q14H C64505 = Q15H C64506 = Q16H C64507 = Q17H C64508 = Q18H C64509 = Q19H C64510 = QH C64511 = Q20H C64512 = Q21H C64513 = Q22H	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C64514 = Q23H C64515 = Q24H C64516 = Q2H C64517 = Q3H C64518 = Q4H C64519 = Q5H C64520 = Q6H C64521 = Q7H C64523 = Q8H C64524 = Q9H C64525 = QOD C64527 = TID C64530 = QID C64533 = Q3D C64534 = Q4D C64535 = Q3S C64536 = Q2M C64537 = Q3M C64538 = Q4M C64576 = ONCE	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C71124 = Q5D C71129 = BIM C71325 = INTERMITTENT C25473 = QD C64954 = OCCASIONAL C64636 = AD LIBITUM C64526 = 1 TIME PER WEEK C98861 = 2 TIMES PER YEAR C98859 = 3 TIMES PER MONTH C98860 = 3 TIMES PER YEAR C98852 = 4 TIMES PER MONTH C98853 = 4 TIMES PER YEAR C98849 = 5 TIMES PER DAY C98850 = 5 TIMES PER MONTH C85552 = 5 TIMES PER WEEK	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C98851 = 5 TIMES PER YEAR C98855 = 6 TIMES PER DAY C98856 = 6 TIMES PER MONTH C98857 = 6 TIMES PER WEEK C98858 = 6 TIMES PER YEAR C98854 = 7 TIMES PER WEEK C74924 = PA C89788 = Q6S C17998 = UNKNOWN C67069 = EVERY WEEK C71127 = EVERY 2 WEEKS C64529 = EVERY 4 WEEKS X0018001 = QAM X0018002 = QPM C64497_1 = 2 TIMES PER WEEK	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C64528_1 = 3 TIMES PER WEEK C64531_1 = 4 TIMES PER WEEK	
(12) CMROUTE	$10		C38192 = AURICULAR (OTIC) C38193 = BUCCAL C38194 = CONJUNCTIVAL C38675 = CUTANEOUS C38197 = DENTAL C38633 = ELECTRO-OSMOSIS C38205 = ENDOCERVICAL C38206 = ENDOSINUSIAL C38208 = ENDOTRACHEAL C38209 = ENTERAL C38210 = EPIDURAL C38211 = EXTRA-AMNIOTIC	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C38212 = EXTRACORPOREAL C38200 = HEMODIALYSIS C38215 = INFILTRATION C38219 = INTERSTITIAL C38220 = INTRA-ABDOMINAL C38221 = INTRA-AMNIOTIC C38222 = INTRA-ARTERIAL C38223 = INTRA-ARTICULAR C38224 = INTRABILIARY C38225 = INTRABRONCHIAL C38226 = INTRABURSAL C38227 = INTRACARDIAC C38228 = INTRACARTILAGINOUS	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C38229 = INTRACAUDAL C38230 = INTRACAVERNOUS C38231 = INTRACAVITARY C38232 = INTRACEREBRAL C38233 = INTRACISTERNAL C38234 = INTRACORNEAL C38217 = INTRACORONAL, DENTAL C38218 = INTRACORONARY C38235 = INTRACORPORUS CAVERNOSUM C38238 = INTRADERMAL C38239 = INTRADISCAL C38240 = INTRADUCTAL	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C38241 = INTRADUODENAL C38242 = INTRADURAL C38243 = INTRAEPIDERMAL C38245 = INTRAESOPHAGEAL C38246 = INTRAGASTRIC C38247 = INTRAGINGIVAL C38249 = INTRAILEAL C38250 = INTRALESIONAL C38251 = INTRALUMINAL C38252 = INTRALYMPHATIC C38253 = INTRAMEDULLARY C38254 = INTRAMENINGEAL C28161 = INTRAMUSCULAR	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C38255 = INTRAOCULAR C38256 = INTRAOVARIAN C38257 = INTRAPERICARDIAL C38258 = INTRAPERITONEAL C38259 = INTRAPLEURAL C38260 = INTRAPROSTATIC C38261 = INTRAPULMONARY C38262 = INTRASINAL C38263 = INTRASPINAL C38264 = INTRASYNOVIAL C38265 = INTRATENDINOUS C38266 = INTRATESTICULAR C38267 = INTRATHECAL	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C38207 = INTRATHORACIC C38268 = INTRATUBULAR C38269 = INTRATUMOR C38270 = INTRATYMPANIC C38272 = INTRAUTERINE C38273 = INTRAVASCULAR C38276 = INTRAVENOUS C38274 = INTRAVENOUS BOLUS C38279 = INTRAVENOUS DRIP C38277 = INTRAVENTRICULAR C38278 = INTRAVESICAL C38280 = INTRAVITREAL C38203 = IONTOPHORESIS	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C38281 = IRRIGATION C38282 = LARYNGEAL C38284 = NASAL C38285 = NASOGASTRIC C48623 = NOT APPLICABLE C38286 = OCCLUSIVE DRESSING TECHNIQUE C38287 = OPHTHALMIC C38288 = ORAL C38289 = OROPHARYNGEAL C38291 = PARENTERAL C38676 = PERCUTANEOUS C38292 = PERIARTICULAR C38677 = PERIDURAL C38293 = PERINEURAL	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C38294 = PERIODONTAL C38295 = RECTAL C38216 = RESPIRATORY (INHALATION) C38296 = RETROBULBAR C38198 = SOFT TISSUE C38297 = SUBARACHNOID C38298 = SUBCONJUNCTIVAL C38299 = SUBCUTANEOUS C38300 = SUBLINGUAL C38301 = SUBMUCOSAL C38304 = TOPICAL C38305 = TRANSDERMAL C38283 = TRANSMUCOSAL	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C38307 = TRANSPLACENTAL C38308 = TRANSTRACHEAL C38309 = TRANSTYMPANIC C38310 = UNASSIGNED C38312 = URETERAL C38271 = URETHRAL C38313 = VAGINAL C78373 = DIETARY C78374 = ORAL GAVAGE C65138 = INTRASTOMAL C102399 = INTRAJEJUNAL C102400 = INTRAPALATAL C38311 = UNKNOWN C17649 = OTHER	
13 M_QVAL_ROUTEOTH	$200			

	Field Name	Data Type	Units	Values	Pre-Filled Values
14	M_CMSTDAT	dd-/MMM-/yyyy			
15	X_CMSTDATUN	1			
16	M_CMPRRFST	$10		C49488 = Yes C49487 = No	
17	M_CMONGO	$10		C49488 = Yes C49487 = No	
18	M_CMENDAT	dd-/MMM-/yyyy			
19	X_CMENDATUN	1			

Was the physical examination performed? (1)

- Yes ☐
- No ☐

What is the date of physical examination? (2) _____

Provide assessment for each organ as compared to the last Physical Exam.

Spleen (4)

- NORMAL ☐
- ABNORMAL ☐
- ENLARGED ☐
- ENLARGED AND DECREASED ☐
- ENLARGED AND INCREASED ☐
- ENLARGED AND STABLE ☐
- NOT DONE ☐

Liver (5)

- NORMAL ☐
- ABNORMAL ☐
- ENLARGED ☐
- ENLARGED AND DECREASED ☐
- ENLARGED AND INCREASED ☐
- ENLARGED AND STABLE ☐
- NOT DONE ☐

Lymph Node (6)

- NORMAL ☐
- ABNORMAL ☐
- ENLARGED ☐
- ENLARGED AND DECREASED ☐
- ENLARGED AND INCREASED ☐
- ENLARGED AND STABLE ☐
- NOT DONE ☐

If lymphadenopathy is present, provide the lymph node location (7)

- ☐ AXILLARY LYMPH NODE
- ☐ OCCIPITAL LYMPH NODE
- ☐ PREAURICULAR LYMPH NODE
- ☐ SUPRACLAVICULAR LYMPH NODE
- ☐ UPPER CERVICAL LYMPH NODE
- ☐ EPITROCHLEAR LYMPH NODE
- ☐ BRACHIAL LYMPH NODE
- ☐ HILAR LYMPH NODE
- ☐ COMMON ILIAC LYMPH NODE
- ☐ INFRACLAVICULAR LYMPH NODE
- ☐ INGUINAL LYMPH NODE
- ☐ FEMORAL LYMPH NODE
- ☐ MEDIASTINAL LYMPH NODE
- ☐ MESENTERIC LYMPH NODE
- ☐ PARA-AORTIC LYMPH NODE
- ☐ POPLITEAL LYMPH NODE
- ☐ SPLENIC HILAR LYMPH NODE
- ☐ WALDEYER'S TONSILLAR RING
- ☐ SUBMANDIBULAR LYMPH NODE
- ☐ PARATRACHEAL LYMPH NODE
- ☐ SUBCARINAL LYMPH NODE
- ☐ RETROPERITONEAL LYMPH NODE
- ☐ RETROCRURAL LYMPH NODE
- ☐ OTHER

Specify if lymph node location is **Other**. _____ (8)

Were symptoms of CNS involvement detected? (9)

- ☐ Yes
- ☐ No

Other Organ

- ABDOMINAL CAVITY ☐ 10
- ADRENAL GLAND ☐
- BONE ☐
- BRAIN ☐
- BREAST ☐
- COLON ☐
- DUODENUM ☐
- HEAD ☐
- JEJUNUM ☐
- KIDNEY ☐
- LIVER ☐
- LUNG ☐
- NECK ☐
- OVARY ☐
- PANCREAS ☐
- PROSTATE GLAND ☐
- RECTUM ☐
- SKIN ☐
- SMALL INTESTINE ☐
- SPLEEN ☐
- STOMACH ☐
- HEART ☐
- TESTES ☐
- UTERUS ☐
- CERVIX UTERI ☐
- ILEUM ☐
- GALLBLADDER ☐
- ESOPHAGUS ☐
- ETHMOID BONE ☐
- ETHMOID SINUS ☐
- OTHER ☐

Specify if Other Organ is **Other**. _____ 11

Other Organ Assessment	NORMAL ☐ 12 ABNORMAL ☐ ENLARGED ☐ ENLARGED AND DECREASED ☐ ENLARGED AND INCREASED ☐ ENLARGED AND STABLE ☐ NOT DONE ☐

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	M_PEPERF	$10		C49488 = Yes C49487 = No	
2	M_PEDAT	dd-/MMM-/yyyy			
4	M_PEORRES_SPLEEN	$10		C14165 = NORMAL C25401 = ABNORMAL X0224001 = ENLARGED X0224002 = ENLARGED AND DECREASED X0224003 = ENLARGED AND INCREASED X0224004 = ENLARGED AND STABLE C49484 = NOT DONE	
5	M_PEORRES_LIVER	$10		C14165 = NORMAL C25401 = ABNORMAL X0224001 = ENLARGED X0224002 = ENLARGED AND DECREASED	

	Field Name	Data Type	Units	Values	Pre-Filled Values
				X0224003 = ENLARGED AND INCREASED X0224004 = ENLARGED AND STABLE C49484 = NOT DONE	
6	M_PEORRES_LYMPH	$10		C14165 = NORMAL C25401 = ABNORMAL X0224001 = ENLARGED X0224002 = ENLARGED AND DECREASED X0224003 = ENLARGED AND INCREASED X0224004 = ENLARGED AND STABLE C49484 = NOT DONE	
7	PELOC_LYMPH	$10		C12904 = AXILLARY LYMPH NODE	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C98188 = OCCIPITAL LYMPH NODE C103429 = PREAURICULAR LYMPH NODE C12903 = SUPRACLAVICULAR LYMPH NODE C103447 = UPPER CERVICAL LYMPH NODE C98182 = EPITROCHLEAR LYMPH NODE C92221 = BRACHIAL LYMPH NODE C98187 = HILAR LYMPH NODE C103384 = COMMON ILIAC LYMPH NODE C63705 = INFRACLAVICULAR LYMPH NODE	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C32801 = INGUINAL LYMPH NODE C98183 = FEMORAL LYMPH NODE C33073 = MEDIASTINAL LYMPH NODE C77641 = MESENTERIC LYMPH NODE C77643 = PARA-AORTIC LYMPH NODE C53146 = POPLITEAL LYMPH NODE C33600 = SPLENIC HILAR LYMPH NODE C73468 = WALDEYER'S TONSILLAR RING C77650 = SUBMANDIBULAR LYMPH NODE	

	Field Name	Data Type	Units	Values	Pre-Filled Values
				C103426 = PARATRACHEAL LYMPH NODE C117873 = SUBCARINAL LYMPH NODE C98189 = RETROPERITONEAL LYMPH NODE C103439 = RETROCRURAL LYMPH NODE C17649 = OTHER	
8	M_QVAL_PELOCOTH	$200			
9	M_QVAL_CNSINVOL	$10		C49488 = Yes C49487 = No	
10	PETEST	$10		C12664 = ABDOMINAL CAVITY C12666 = ADRENAL GLAND C12366 = BONE C12439 = BRAIN	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C12971 = BREAST C12382 = COLON C12263 = DUODENUM C12419 = HEAD C12388 = JEJUNUM C12415 = KIDNEY C12392 = LIVER C12468 = LUNG C13063 = NECK C12404 = OVARY C12393 = PANCREAS C12410 = PROSTATE GLAND C12390 = RECTUM C12470 = SKIN C12386 = SMALL INTESTINE C12432 = SPLEEN C12391 = STOMACH C12727 = HEART X0123001 = TESTES	

	Field Name	Data Type	Units	Values	Pre-Filled Values
				C12405 = UTERUS C12311 = CERVIX UTERI C12387 = ILEUM C12377 = GALLBLADDER C12389 = ESOPHAGUS C12711 = ETHMOID BONE C12276 = ETHMOID SINUS C17649 = OTHER	
11	M_QVAL_PE TESTOT	$200			
12	M_PEORRES _OTHER	$10		C14165 = NORMAL C25401 = ABNORMAL X0224001 = ENLARGED X0224002 = ENLARGED AND DECREASED X0224003 = ENLARGED AND INCREASED	

Field Name	Data Type	Units	Values	Pre-Filled Values
			X0224004 = ENLARGED AND STABLE C49484 = NOT DONE	

Initial MCL Diagnosis

Diagnosis	MANTLE CELL LYMPHOMA (2)
Category for Medical History	RELAPSED OR REFRACTORY MANTLE CELL LYMPHOMA (3)
Reported Term for the Medical History	RELAPSED OR REFRACTORY MANTLE CELL LYMPHOMA (4)
What was the date of the diagnosis (Initial)?	_____ (5)
Are B-symptoms present?	Yes (6) No Unknown
t(14;18)	NEGATIVE (7) POSITIVE INDETERMINATE
Cyclin D1	NEGATIVE (8) POSITIVE INDETERMINATE
MIPI Score	LOW RISK (9) INTERMEDIATE RISK HIGH RISK UNKNOWN
What is the Ann Arbor Stage?	STAGE I (10) STAGE II

STAGE III ☐
STAGE IV ☐
UNKNOWN ☐

Bulky Disease (>= 7 cm in single dimension)? 11

Yes ☐
No ☐
Unknown ☐

Did the subject have high tumor burden at initial diagnosis? 12

Yes ☐
No ☐
Unknown ☐

Specify if other abnormalities were noted? _____ 13

	Field Name	Data Type	Units	Values	Pre-Filled Values
2	MHTERM_DLBCL	$10		X0430008 = MANTLE CELL LYMPHOMA	
3	MHCAT_MM	$10		X0176004 = RELAPSED OR REFRACTORY MANTLE CELL LYMPHOMA	
4	MHTERM_DISDX	$10		X0177004 = RELAPSED OR REFRACTORY MANTLE CELL LYMPHOMA	
5	M_MHSTDAT	dd-/MMM-/yyyy			
6	M_FAORRES_OCCUR_BSP	$10		C49488 = Yes C49487 = No C17998 = Unknown	
7	M_PFORRES_T14S18	$10		C38757 = NEGATIVE C38758 = POSITIVE C48658 = INDETERMINATE	

	Field Name	Data Type	Units	Values	Pre-Filled Values
8	M_PFORRES_CD1	$10		C38757 = NEGATIVE C38758 = POSITIVE C48658 = INDETERMINATE	
9	M_FAORRES_MIPI	$10		C102403 = LOW RISK C102402 = INTERMEDIATE RISK C102401 = HIGH RISK C17998 = UNKNOWN	
10	M_FAORRES_AAS	$10		X0437001 = STAGE I X0437002 = STAGE II X0437003 = STAGE III X0437004 = STAGE IV C17998 = UNKNOWN	
11	M_FAORRES_OCCUR_BD	$10		C49488 = Yes C49487 = No C17998 = Unknown	
12	M_FAORRES_OCCUR_HTB	$10		C49488 = Yes C49487 = No	

	Field Name	Data Type	Units	Values	Pre-Filled Values
				C17998 = Unknown	
13	M_PFTEST_OTH	$100			

Relapse or Refractory MCL Diagnosis

Diagnosis	MANTLE CELL LYMPHOMA ☐ 2
Category for Medical History	RELAPSED OR REFRACTORY MANTLE CELL LYMPHOMA ☐ 3
Reported Term for the Medical History	RELAPSED OR REFRACTORY MANTLE CELL LYMPHOMA ☐ 4
What was the date of the diagnosis (Relapse or Refractory)?	_____ 5
Are B-symptoms present?	Yes ☐ 6 No ☐ Unknown ☐
t(14;18)	NEGATIVE ☐ 7 POSITIVE ☐ INDETERMINATE ☐
Cyclin D1	NEGATIVE ☐ 8 POSITIVE ☐ INDETERMINATE ☐
MIPI Score	LOW RISK ☐ 9 INTERMEDIATE RISK ☐ HIGH RISK ☐ UNKNOWN ☐
What is the Ann Arbor Stage?	STAGE I ☐ 10 STAGE II ☐

STAGE III ☐
STAGE IV ☐
UNKNOWN ☐

Bulky Disease (>= 7 cm in single dimension)? 11

Yes ☐
No ☐
Unknown ☐

Did the subject have high tumor burden at relapse/refractory disease? 12

Yes ☐
No ☐
Unknown ☐

Specify if other abnormalities were noted? _____ 13

	Field Name	Data Type	Units	Values	Pre-Filled Values
2	MHTERM_DLBCL	$10		X0430008 = MANTLE CELL LYMPHOMA	1: MANTLE CELL LYMPHOMA
3	MHCAT_MM	$10		X0176004 = RELAPSED OR REFRACTORY MANTLE CELL LYMPHOMA	1: RELAPSED OR REFRACTORY MANTLE CELL LYMPHOMA
4	MHTERM_DISDX	$10		X0177004 = RELAPSED OR REFRACTORY MANTLE CELL LYMPHOMA	1: RELAPSED OR REFRACTORY MANTLE CELL LYMPHOMA
5	M_MHSTDAT	dd-/MMM-/yyyy			
6	M_FAORRES_OCCUR_BSP	$10		C49488 = Yes C49487 = No C17998 = Unknown	
7	M_PFORRES_T14S18	$10		C38757 = NEGATIVE C38758 = POSITIVE C48658 = INDETERMINATE	

	Field Name	Data Type	Units	Values	Pre-Filled Values
8	M_PFORRES_CD1	$10		C38757 = NEGATIVE C38758 = POSITIVE C48658 = INDETERMINATE	
9	M_FAORRES_MIPI	$10		C102403 = LOW RISK C102402 = INTERMEDIATE RISK C102401 = HIGH RISK C17998 = UNKNOWN	
10	M_FAORRES_AAS	$10		X0437001 = STAGE I X0437002 = STAGE II X0437003 = STAGE III X0437004 = STAGE IV C17998 = UNKNOWN	
11	M_FAORRES_OCCUR_BD	$10		C49488 = Yes C49487 = No C17998 = Unknown	
12	M_FAORRES_OCCUR_HTB	$10		C49488 = Yes C49487 = No	

	Field Name	Data Type	Units	Values	Pre-Filled Values
				C17998 = Unknown	
13	M_PFTEST_OTH	$100			

Were there any prior systemic anti-cancer therapies for this disease?

Yes ☐ 1
No ☐

Were there any prior stem cell transplants for this disease?

Yes ☐ 2
No ☐

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	X_SACYN	$10		C49488 = Yes C49487 = No	
2	X_SCTYN	$10		C49488 = Yes C49487 = No	

Line of Therapy Number	_____	1
What was the best response for the line of therapy?	Progressive Disease ☐ Stable Disease ☐ Partial Response ☐ Complete Response ☐ UNKNOWN ☐	2
What was the date of best response?	_____	3
Check if the date of best response is unknown	_____	4
Did the disease progress during or after this line of therapy, but prior to starting next line of therapy?	Yes ☐ No ☐	5
If the disease progressed or relapsed, provide the date of progression or relapse.	_____	6
Check if the date of relapse is unknown	_____	7
What was the reason for discontinuing the line of therapy?	PROGRESSIVE DISEASE ☐ TOXICITY ☐ COMPLETED ☐ WITHDRAWAL BY SUBJECT ☐ OTHER ☐	8
Specify if reason for discontinuing the line of therapy is 'Other'	_____	9
What was the term for the medication taken?	_____	10
Type of Anti-Lymphoma Therapy	INDUCTION ☐	11

	CONSOLIDATION ☐ CONDITIONING ☐ MAINTENANCE ☐ OTHER ☐
Is the number of cycles known?	Yes ☐ 12 No ☐
If yes, enter number of cycles.	_____ 13
What was the start date of the medication/therapy?	_____ 14
Check if the date is unknown	_____ 15
What was the end date of the medication/therapy?	_____ 16
Is the medication/therapy still ongoing?	Yes ☐ 17 No ☐
Check if the end date is unknown	_____ 18

0008 CC-5013-MCL-005_CPPC2: UNIQUE
Project Name: CC-5013-MCL-005
Form: Prior Medications - Systemic Anti-Cancer Therapies
Generated On: 23 Oct 2020 11:54:19

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	M_QVAL_LINETHX	2			
2	M_QVAL_BESTRESP	$10		C35571 = Progressive Disease C18213 = Stable Disease C18058 = Partial Response C4870 = Complete Response C17998 = UNKNOWN	
3	M_QVAL_BSRSPDAT	dd-/MMM-/yyyy			
4	X_QVALDATUN	1			
5	X_CMPRGYN	$10		C49488 = Yes C49487 = No	
6	M_QVAL_CMPDDAT	dd-/MMM-/yyyy			
7	X_QVALDATUN_S01	1			

	Field Name	Data Type	Units	Values	Pre-Filled Values
8	M_QVAL_CMDSRGM	$10		C35571 = PROGRESSIVE DISEASE X0152001 = TOXICITY C25250 = COMPLETED C49634 = WITHDRAWAL BY SUBJECT C17649 = OTHER	
9	M_QVAL_DSRGMOTH	$200			
10	CMTRT	$200			
11	M_QVAL_CMTYPE	$10		X0149003 = INDUCTION X0149004 = CONSOLIDATION X0149005 = CONDITIONING X0149007 = MAINTENANCE C17649 = OTHER	
12	X_CMCYCYN	$10		C49488 = Yes C49487 = No	

	Field Name	Data Type	Units	Values	Pre-Filled Values
13	M_QVAL_CMCYCNUM	2			
14	M_CMSTDAT	dd-/MMM-/yyyy			
15	X_CMSTDAT1UN	1			
16	M_CMENDAT	dd-/MMM-/yyyy			
17	M_CMONGO	$10		C49488 = Yes C49487 = No	
18	X_CMENDATUN	1			

Procedure Category	STEM CELL TRANSPLANTS FOR DISEASE UNDER STUDY (1)
Procedure	_____ (2)
Type of Stem Cell Transplant	AUTOLOGOUS (3) ALLOGENEIC
What was the start date of the Transplantation?	_____ (4)
When did the therapy/procedure start relative to the first dose of study drug/informed consent?	BEFORE (5) DURING/AFTER AFTER DURING
What was the best response?	Progressive Disease (6) Stable Disease Partial Response Complete Response UNKNOWN

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	M_PRCAT	$10		X0157003 = STEM CELL TRANSPLANTS FOR DISEASE UNDER STUDY	
2	M_PRTRT	$200			
3	M_QVAL_PRTYPE	$10		X0163001 = AUTOLOGOUS X0163002 = ALLOGENEIC	
4	M_PRSTDAT	dd-/MMM-/yyyy			
5	PRSTRF	$10		C25629 = BEFORE C49640 = DURING/AFTER C38008 = AFTER C25490 = DURING	
6	M_QVAL_BESTRESP	$10		C35571 = Progressive Disease C18213 = Stable Disease	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C18058 = Partial Response C4870 = Complete Response C17998 = UNKNOWN	

Was the dose administered? Yes ☐ No ☐ (1)

Reason if dose was not administered. ADVERSE EVENT ☐ ADVERSE EVENT - NOT TO BE RECORDED ☐ INVESTIGATOR DECISION ☐ PERMANENTLY DISCONTINUED DUE TO PROGRESSIVE DISEASE ☐ REST PERIOD ☐ OTHER ☐ (2)

Specify the other reason why dose was not administered. _____ (3)

What was the start date? _____ (4)

What was the stop date? _____ (5)

Ongoing? Yes ☐ (6)

What was the study treatment? LENALIDOMIDE ☐ (7)

Was the dose adjusted from previous dose? Yes ☐ No ☐ (8)

What was the reason the dose was adjusted? ADVERSE EVENT ☐ ADVERSE EVENT - NOT TO BE RECORDED ☐ INVESTIGATOR DECISION ☐ OTHER ☐ (9)

Specify the other reason for dose adjustment _____ 10

What was the actual dose administered? _____ 11

What were the units for the dose? mg ☐ 12

CF trigger used in CF _____ 13

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	M_ECOCCUR	$10		C49488 = Yes C49487 = No	
2	M_QVAL_ECREND	$10		1 = ADVERSE EVENT 14 = ADVERSE EVENT - NOT TO BE RECORDED 4 = INVESTIGATOR DECISION 15 = PERMANENTLY DISCONTINUED DUE TO PROGRESSIVE DISEASE 16 = REST PERIOD C17649 = OTHER	
3	M_QVAL_ECRENDOT	$200			
4	M_ECSTDAT	dd-/MMM-/yyyy			
5	M_ECENDAT	dd-/MMM-/yyyy			

	Field Name	Data Type	Units	Values	Pre-Filled Values
6	M_ECONGO	$10		C49488 = Yes	
7	ECTRT	$10		LEN = LENALIDOMIDE	1: LENALIDOMIDE
8	M_ECDOSADJ	$10		C49488 = Yes C49487 = No	
9	ECADJ	$10		1 = ADVERSE EVENT 14 = ADVERSE EVENT - NOT TO BE RECORDED 4 = INVESTIGATOR DECISION C17649 = OTHER	
10	M_ECADJOTH	$200			
11	ECDOSE	6.2			
12	ECDOSU	$10		C28253 = mg	1: mg
13	DX_CFTRIGGER	dd MMM yyyy hh:nn:ss			

Check not done if best overall response assessment was not performed.

NOT DONE ☐ 1

What is the category for response assessment? 2

- ☐ CHESON 1999
- ☐ CHESON 2007
- ☐ CHESON 2014

What is the method of assessment? 3

- ☐ CT SCAN
- ☐ ENDOSCOPY
- ☐ MRI
- ☐ PET/CT SCAN
- ☐ PHYSICAL EXAMINATION
- ☐ OTHER

Specify, if method of assessment is 'Other' 4 _____

What was the date of disease response assessment? 5 _____

What is the best overall response? 6

- ☐ Progressive Disease
- ☐ Stable Disease
- ☐ Partial Response
- ☐ Complete Response
- ☐ Not Evaluable

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	M_RSSTAT_BESTRESP	$10		C49484 = NOT DONE	
2	RSCAT	$10		X0136016 = CHESON 1999 X0136003 = CHESON 2007 X0136009 = CHESON 2014	
3	M_RSMETHOD	$10		C17204 = CT SCAN C16546 = ENDOSCOPY C16809 = MRI C103512 = PET/CT SCAN C20989 = PHYSICAL EXAMINATION C17649 = OTHER	
4	M_QVAL_METHDOTH	$200			
5	M_RSDAT	dd-/MMM-/yyyy			

	Field Name	Data Type	Units	Values	Pre-Filled Values
6	M_RSORRES_BESTRESP	$10		C35571 = Progressive Disease C18213 = Stable Disease C18058 = Partial Response C4870 = Complete Response C62222 = Not Evaluable	

Was the assessment performed? ☐ Yes (1) ☐ No

Were there any lesions identified to report? ☐ Yes (2) ☐ No

What is the lesion number? _____ (3)

What is the date of lesion identification? _____ (4)

What is the location of the lesion? (5)

- ☐ ABDOMINAL CAVITY
- ☐ ADRENAL GLAND
- ☐ AXILLARY LYMPH NODE
- ☐ BONE
- ☐ BRACHIAL LYMPH NODE
- ☐ BRAIN
- ☐ BREAST
- ☐ CERVICAL LYMPH NODE
- ☐ CERVICAL VERTEBRA
- ☐ CERVIX UTERI
- ☐ CHEST
- ☐ COLON
- ☐ DUODENUM
- ☐ EPITROCHLEAR LYMPH NODE
- ☐ ESOPHAGUS
- ☐ ETHMOID BONE
- ☐ ETHMOID SINUS
- ☐ FEMORAL LYMPH NODE
- ☐ GALL BLADDER
- ☐ HEAD
- ☐ HEART
- ☐ HILAR LYMPH NODE

- [ ] ILEUM
- [ ] ILIAC LYMPH NODE
- [ ] INFRACLAVICULAR LYMPH NODE
- [ ] INGUINAL LYMPH NODE
- [ ] JEJUNUM
- [ ] KIDNEY
- [ ] LEPTOMENINGES
- [ ] LIVER
- [ ] LOWER EXTREMITY
- [ ] LUMBAR VERTEBRA
- [ ] LUNG
- [ ] LYMPH NODE
- [ ] MEDIASTINAL LYMPH NODE
- [ ] MESENTERIC LYMPH NODE
- [ ] NECK
- [ ] OCCIPITAL LYMPH NODE
- [ ] OTHER
- [ ] OVARY
- [ ] PANCREAS
- [ ] PARAAORTIC LYMPH NODE
- [ ] PARATRACHEAL LYMPH NODE
- [ ] PELVIS
- [ ] POPLITEAL LYMPH NODE
- [ ] PREAURICULAR LYMPH NODE
- [ ] PROSTATE GLAND
- [ ] RECTUM
- [ ] RETROCRURAL LYMPH NODE
- [ ] RETROPERITONEAL LYMPH NODE
- [ ] SKIN
- [ ] SKULL
- [ ] SMALL INTESTINE
- [ ] SPINAL CORD

SPLEEN ☐
SPLENIC HILAR LYMPH NODE ☐
STOMACH ☐
SUBCARINAL LYMPH NODE ☐
SUBMANDIBULAR LYMPH NODE ☐
SUPRACLAVICULAR LYMPH NODE ☐
TESTIS ☐
THORACIC VERTEBRA ☐
UPPER EXTREMITY ☐
UTERUS ☐
WALDEYER'S TONSILLAR RING ☐

Specify if location is **Other**. _____ 6

What is the method of lesion identification? 7

CT SCAN ☐
ENDOSCOPY ☐
MRI ☐
PET/CT SCAN ☐
PHYSICAL EXAMINATION ☐
OTHER ☐

Specify if method of lesion identification is "Other" _____ 8

Bulky Disease (>= 7 cm in single dimension)? 9

Yes ☐
No ☐

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	X_TUPERF	$10		C49488 = Yes C49487 = No	
2	X_LESIDEN	$10		C49488 = Yes C49487 = No	
3	TULNKID	$10			
4	M_TUDAT	dd-/MMM-/yyyy			
5	TULOC_GEN	$10		C12664 = ABDOMINAL CAVITY C12666 = ADRENAL GLAND C12904 = AXILLARY LYMPH NODE C12366 = BONE C92221 = BRACHIAL LYMPH NODE C12439 = BRAIN C12971 = BREAST C32298 = CERVICAL LYMPH NODE	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C12693 = CERVICAL VERTEBRA C12311 = CERVIX UTERI C25389 = CHEST C12382 = COLON C12263 = DUODENUM C98182 = EPITROCHL EAR LYMPH NODE C12389 = ESOPHAGUS C12711 = ETHMOID BONE C12276 = ETHMOID SINUS C98183 = FEMORAL LYMPH NODE C12377 = GALL BLADDER C12419 = HEAD C12727 = HEART C98187 = HILAR LYMPH NODE	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C12387 = ILEUM C32761 = ILIAC LYMPH NODE C63705 = INFRACLAVICULAR LYMPH NODE C32801 = INGUINAL LYMPH NODE C12388 = JEJUNUM C12415 = KIDNEY X0150001 = LEPTOMENINGES C12392 = LIVER X74456001 = LOWER EXTREMITY C12744 = LUMBAR VERTEBRA C12468 = LUNG C12745 = LYMPH NODE C33073 = MEDIASTINAL LYMPH NODE	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C77641 = MESENTERIC LYMPH NODE C13063 = NECK C98188 = OCCIPITAL LYMPH NODE C17649 = OTHER C12404 = OVARY C12393 = PANCREAS C77643 = PARAAORTIC LYMPH NODE C103426 = PARATRACHEAL LYMPH NODE C12767 = PELVIS C53146 = POPLITEAL LYMPH NODE C103429 = PREAURICULAR LYMPH NODE C12410 = PROSTATE GLAND	

Field Name	Data Type	Units	Values	Pre-Filled Values
			C12390 = RECTUM C103439 = RETROCRURAL LYMPH NODE C98189 = RETROPERITONEAL LYMPH NODE C12470 = SKIN C12789 = SKULL C12386 = SMALL INTESTINE C12464 = SPINAL CORD C12432 = SPLEEN C33600 = SPLENIC HILAR LYMPH NODE C12391 = STOMACH C117873 = SUBCARINAL LYMPH NODE C77650 = SUBMANDIBULAR LYMPH NODE	

	Field Name	Data Type	Units	Values	Pre-Filled Values
				C12903 = SUPRACLAVICULAR LYMPH NODE C12412 = TESTIS C12798 = THORACIC VERTEBRA X74456002 = UPPER EXTREMITY C12405 = UTERUS C73468 = WALDEYER'S TONSILLAR RING	
6	M_QVAL_TU$200 LOCOTH				
7	TUMETHOD	$10		C17204 = CT SCAN C16546 = ENDOSCOPY C16809 = MRI C103512 = PET/CT SCAN C20989 = PHYSICAL EXAMINATION	

	Field Name	Data Type	Units	Values	Pre-Filled Values
				C17649 = OTHER	
8	M_QVAL_METHDOTH	$200			
9	M_QVAL_BDGE7CM	$10		C49488 = Yes C49487 = No	

What is the procedure?		1
What was the start date of the procedure?		2
Check if the start date is unknown.		3
What was the end date of the procedure?		4
Check if the end date is unknown.		5
What was the **primary** reason the procedure was performed?	ADVERSE EVENT ☐ MEDICAL HISTORY ☐ OTHER ☐	6
If the primary reason for the procedure is AE or MH, select the ID of the primary event.		7
If the primary reason for the procedure is **other** than AE or MH, enter the primary term of the indication.		8
If there are additional AEs that are indications for this procedure, enter the AE ID separated by semicolons (;)		9
If there are additional MH events that are indications for this procedure, enter the MH ID separated by semicolons (;)		10
If there are additional indications for this procedure that are not AEs or MH, enter the indications separated by semicolons (;)		11

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	PRTRT	$200			
2	M_PRSTDAT	dd-/MMM-/yyyy			
3	X_PRSTDAT_UN	1			
4	M_PRENDAT	dd-/MMM-/yyyy			
5	X_PRSTDAT_UN_S01	1			
6	M_PRINDCAT	$10		1 = ADVERSE EVENT 2 = MEDICAL HISTORY C17649 = OTHER	
7	M_PRINDC_AEMH	$120			
8	M_PRINDC_OTH	$200			
9	M_IDVARVAL_AESPID	$40			

0008 CC-5013-MCL-005_CPPC2: UNIQUE
Project Name: CC-5013-MCL-005
Form: Prior and Concomitant Procedures
Generated On: 23 Oct 2020 11:54:19

	Field Name	Data Type	Units	Values	Pre-Filled Values
10	M_IDVARVA L_MHSPID	$40			
11	M_QVAL_PR INDCO	$200			

Date of subject characteristics collection	1
Enter age at time of first Lenalidomide dose	2

0008 CC-5013-MCL-005_CPPC2: UNIQUE
Project Name: CC-5013-MCL-005
Form: Subject Characteristics
Generated On: 23 Oct 2020 11:54:19

	Field Name	Data Type	Units	Values	Pre-Filled Values
1	M_SCDAT	dd-/MMM-/yyyy			
2	M_SCORRES_AGE	3			

APPENDIX 1.3 Informed Consent Forms

8 page(s) excluding cover page

Approved v1.0 930231036 1.0

APPENDIX 1.3 Informed Consent Forms

- Informed Consent Form

RESEARCH SUBJECT INFORMED CONSENT FORM

Study Title:	A Non-interventional, Post-authorization Safety Study of Patients with Relapsed or Refractory Mantle Cell Lymphoma to Further Investigate and Characterize the Association of Lenalidomide With Tumor Flare Reaction and High Tumor Burden (MCL-005 study)
Protocol Number	CC-5013-MCL-005
Protocol version identifier:	Version 4.0_28 Aug 2019
Procedure Number:	EMEA/H/C/000717/MEA/046.2
Marketing authorization holder:	[redacted]
Sponsor:	[redacted]
Doctor (Investigator):	[redacted]

1. BACKGROUND AND PURPOSE

You are being asked to take part in this study because you have been diagnosed with a relapsed and/refractory mantle cell lymphoma and your doctor has chosen to treat you with lenalidomide (Revlimid®). Lenalidomide has been approved for the treatment of adult patients with relapsed/refractory mantle cell lymphoma (MCL). Relapsed/refractory mantle cell lymphoma is

a mantle cell lymphoma that reappears after a successful prior treatment or that did not improve in response to a prior treatment.

According to what your doctor considers to be the best treatment for you, he/she decided about your treatment before you were proposed to enter this study. The treatment decisions your doctor made will **not** be affected by you taking part in the study.

The purpose of this study is to collect more information about the safety profile of your treatment. It is **not** the purpose of this study to test a new experimental product. This study will **not** have any influence on the treatment or the way your doctor is monitoring your health and treatment. You will, thus, not be asked to take any new experimental or unapproved medicine for this study.

The main purpose of this study is only to collect data on a specific adverse event, namely "tumor flare reaction" (TFR), which may occur in about 10 % of patients receiving treatment with lenalidomide for relapsed and/refractory mantle cell lymphoma. A tumor flare reaction consists often in a sudden swelling of the lymph nodes, fever and moderate pain. It occurs mostly at the first cycle of lenalidomide treatment and can be easily managed with anti-inflammatory drugs and/ or dose adaptation. Tumor flare reactions have been previously described in patient taking lenalidomide for other diseases which are similar to yours: for example, chronic lymphocytic leukemias). It occurred also in patients with other diseases, for example, breast or prostate cancers, who were treated with other drugs.

About 560 patients within Europe will take part in this study.

2. WHAT DOES THE STUDY ENTAIL?

Observational studies are studies in which data are recorded and analyzed that arise in the normal course of patient care.

The purpose of this study is only to collect more information about the safety profile of your treatment, particularly regarding tumor flare reactions. Data collection will focus mainly on the key points of your medical history, including the previous lines of treatment that you received for your mantle cell lymphoma, the current treatment with lenalidomide, and information about changes in your disease and health which may be related to a tumor flare reaction.

This study is a so-called retrospective study. That means that the study doctor will not be recording data specifically for the purpose of the study when you will be visiting him/her. The data which are necessary for the conduct of this study will be retrieved from your existing medical record. Data will only be retrieved for the first 6 months following your first dose of lenalidomide. The data will be retrieved after these six months.

3. VOLUNTARY PARTICIPATION IN THE STUDY

Your participation in this study is voluntary. You can decide not to take part, or to leave the study at any time, for any reason, without penalty or loss of medical care or benefits to which you are entitled. Thus, if you decide not to take part or to stop your participation in the study, we will stop collecting data with respect to your treatment with lenalidomide. It does not mean that you will stop lenalidomide because the purpose of the current study is only to collect data, and not the treatment itself.

Any questions and concerns with respect of the treatment should be discussed with your doctor.

4. PRIVACY AND CONFIDENTIALITY

The study doctor will collect information from you.

The study doctor will keep your medical records and any other record identifying you confidential. To the extent permitted by law, monitors, auditors, and competent authorities - for example, inspectors or other officials of the health authority in your country, the European Medicines Agency (EMA), the United States Food and Drug Administration (FDA) –will have access to your medical records in order to verify the study data and compliance with the study procedures. Those persons will have the obligation to keep your records and the information contained in them confidential.

The study doctor will transfer these data to Celgene or third parties which assist Celgene with the conduct of the study. Before the transfer, your name, ID number or any other information which allows your direct identification will be replaced with a code. Neither Celgene nor the third parties mentioned above will be able to identify you. A confidential list of names will link the code to your name for a period of [insert source document retention period]. Only authorized people (for example, the study doctor) will have access to the list of names and will be able to identify you.

Celgene may share information collected during the study with scientists outside Celgene for other scientific research in the interest of public health. The information collected for the purpose of the study will, in particular, be shared with the Harmony project. Harmony is a joint research initiative of partners from academic, healthcare and public institutions and pharmaceutical industry. All these partners conduct research on multiple myeloma, leukemia, lymphoma and other similar blood diseases. The purpose of this project is to bring a large quantity of research data from these partners together and to analyze it in order to better understand blood diseases like mantle cell lymphoma. The information which Celgene will make available to the Harmony project or other research projects outside the company will be anonymous. That means that Celgene will not provide information about your identity to these projects. No organization or person who is conducting these projects will thus be able to identify you.

The coded study data will only be used for the purposes mentioned above and the follow-up of the safety and the effectiveness of the treatment. Only authorized members of the study doctor's staff, Celgene's personnel or third parties which assist Celgene with the conduct of the study will have access to the data which identify you. Celgene may also disclose the data to competent

authorities. The study doctor will give you the list of third parties who are receiving your coded data if you ask for it.

Celgene may transfer the coded study data outside your country and the European Economic Area (e.g., to the United States) in order to process or to submit them to competent authorities. The data protection requirements which apply in those countries may not provide an adequate protection for your data. Celgene shall nevertheless ensure that the necessary measures are taken in order to protect and maintain the confidentiality of your data. Celgene will in any case provide appropriate safeguards for these transfers of your personal data outside your country or the European Economic Area (e.g. by imposing "Standard Data Protection Contractual Clauses" on recipients of your data or any other measure defined by law). In any event, all parties involved in the study are required to maintain the confidentiality of your personal data.

The study results may be mentioned in medical books or journals or used for teaching purposes. Your identity will not be mentioned. Celgene may also share information collected during the study with scientists outside Celgene for further scientific research in the interest of public health. Celgene will, however, not provide information about your identity to these scientists.

If you leave the study or after your participation has been stopped for any other reason, any information collected while you were in the study will be kept and may be included in the final results of the study.

Under European Union data protection law (the Data Protection Directive, replaced on 25 May 2018 with the General Data Protection Regulation), *[and]* [*insert the name and reference of the applicable data protection law in the country when needed*], both Celgene and your hospital will be considered "data controllers" in the context of the study. That means that Celgene and your hospital have the responsibility to ensure that personal data collected in the course of the study, must be processed in accordance with the law. The hospital will have that responsibility with respect to the study data which have been recorded in your medical record. Celgene will assume that responsibility with respect to the coded study data which the study doctor transferred to Celgene or third parties.

You have the right to access and verify your personal information held by the study doctor or Celgene and to obtain its deletion or correction if it is inaccurate. In certain circumstances, you have the additional rights to object to how your information is being handled, request deletion of your data, restrict aspects of the processing of your information or to ask that a copy of your data be provided to you, or a third party, in a digital format. If you wish to exercise those rights, contact your study doctor in writing (see contact details above). If you have any questions or comments about how your information is handled in this study, you should firstly contact your study doctor. He/she will direct your query to the appropriate staff responsible for data protection at the Celgene or your hospital, including the Data Protection Officer of your hospital.

You also have the right to complain about how your information is handled to a supervisory authority that is responsible for enforcing data protection law. A list of European Union

supervisory authorities is available here: http://ec.europa.eu/justice/data-protection/article-29/structure/data-protection-authorities/index_en.htm.

This study may only be performed by collecting and using personal information on study participants as described in this form. Therefore, you may only participate in the study if you agree to the collection and use of your information as described here.

5. WILL YOU BE PAID FOR YOUR PARTICIPATION IN THE STUDY?

You will not receive any payment for being in the study.

6. IF YOU NEED MORE INFORMATION

Please do not hesitate to contact the study doctor if you have any questions about the study, the procedures, the treatment or your rights, or if you want to review your personal data held by the study doctor. The contact details of the study doctor are mentioned at the top of this document.

If you have questions about your patient rights in the context of the study you can contact: insert name and contact details of the person or organization in accordance with country ICF Guidance.

You can find information about this study on the web page http://www.ClinicalTrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results of the study. You can search this website at any time. [for PASS/PAES studies, they will also be registered and available on the European network of Centers for Pharmacoepidemiology and Pharmacovigilance www.encepp.eu]

INFORMED CONSENT

Feel free to discuss the information in this document with your family, doctor(s) or friends. Do not sign this document until you have had a chance to ask the study doctor or his/her staff all of your questions and all questions have been answered to your satisfaction.

- I agree to participate in the study.
- I understand that I can leave the study at any time.
- I understand and agree that monitors, auditors, the ethics committee, and competent authorities as for example, the European Medicines Agency (EMA) and the United States Food and Drug Administration (FDA), and other competent authorities will have direct access to my medical records in order to verify the study data and compliance with the study procedures.
- I agree that my personal data are collected, processed and transferred outside my country (including outside the European Economic Area) for the purposes of the study and the follow-up of the safety of the treatment. If my participation stops, my personal data may be further processed for the purposes of the study and to follow-up the safety and the effect of the treatment unless I told the study doctor not to do so. Celgene may share information collected during the study with scientists outside Celgene for further scientific research in the interest of public health. Celgene shall however not share information about my identity with these scientists.
- I agree /I do not agree (circle one) that my family doctor can be informed that I am taking part in the study.
- I authorize/I do not authorize (circle one) that if I pass away after I leave the study,
    - (a) the study doctor or the doctor in charge of my treatment tells Celgene about the date and the cause of my death; and
    - (b) Celgene may process this information for the purposes of the study or the follow-up of the safety and the effect of the treatment.
- I have been provided the Pregnancy Prevention Information Sheet and the Study doctor has explained this information to me. I understand and agree to comply with the pregnancy precautions as outlined in the Patient Information Sheet.

_____
Research Subject's Name (Print)

_____ _____
Research Subject's Signature Date of signature

_____ _____
Legally Acceptable Representative (if applicable) Date of signature

_____
Relationship to Subject

I have explained the purpose of this study, the study procedures, the possible risks, discomforts and benefits. I have answered all questions regarding the study to the best of my ability.

_____
Name of Person Obtaining Consent (print)

_____ _____
Signature of Person Obtaining Consent Date of signature

APPENDIX 1.4 List of Investigators

6 page(s) excluding cover page

Approved v1.0 930231036 1.0

APPENDIX 1.4 List of Investigators

- List of Investigators

List of Investigators

Country	Site ID	Principal Investigator [Last name, First Name]	Site Name and Address
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Austria	102	[redacted]	[redacted]
Austria	103	[redacted]	[redacted]
Austria	104	[redacted]	[redacted]
Austria	105	[redacted]	[redacted]
France	303	[redacted]	[redacted]
France	304	[redacted]	[redacted]
France	305	[redacted]	[redacted]
France	308	[redacted]	[redacted]
France	310	[redacted]	[redacted]
France	311	[redacted]	[redacted]

Country	Site ID	Principal Investigator [Last name, First Name]	Site Name and Address
France	312	[redacted]	[redacted]
Germany	252	[redacted]	[redacted]
Germany	253	[redacted]	[redacted]
Germany	255	[redacted]	[redacted]
Germany	256	[redacted]	[redacted]
Greece	501	[redacted]	[redacted]
Greece	502	[redacted]	[redacted]
Greece	503	[redacted]	[redacted]
Greece	506	[redacted]	[redacted]
Greece	508	[redacted]	[redacted]
Greece	509	[redacted]	[redacted]

Country	Site ID	Principal Investigator [Last name, First Name]	Site Name and Address
Greece	510	[redacted]	[redacted]
Greece	511	[redacted]	[redacted]
Italy	601	[redacted]	[redacted]
Italy	602	[redacted]	[redacted]
Italy	603	[redacted]	[redacted]
Italy	604	[redacted]	[redacted]
Italy	605	[redacted]	[redacted]
Italy	606	[redacted]	[redacted]
Italy	607	[redacted]	[redacted]
Italy	608	[redacted]	[redacted]
Italy	609	[redacted]	[redacted]

Country	Site ID	Principal Investigator [Last name, First Name]	Site Name and Address
Italy	610	[redacted]	[redacted]
Italy	611	[redacted]	[redacted]
Italy	613	[redacted]	[redacted]
Italy	614	[redacted]	[redacted]
Italy	615	[redacted]	[redacted]
Italy	616	[redacted]	[redacted]
Italy	617	[redacted]	[redacted]
Netherlands	401	[redacted]	[redacted]
Spain	201	[redacted]	[redacted]
Spain	202	[redacted]	[redacted]
Spain	203	[redacted]	[redacted]
Spain	204	[redacted]	[redacted]

Country	Site ID	Principal Investigator [Last name, First Name]	Site Name and Address
Spain	205	[redacted]	[redacted]
Spain	206	[redacted]	[redacted]
Spain	207	[redacted]	[redacted]

APPENDIX 1.5 Documentation of Statistical Methods

27 page(s) excluding cover page

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APPENDIX 1.5 Documentation of Statistical Methods

- Statistical Analysis Plan Version 2 Dated 16 September 2023

NON-INTERVENTIONAL STATISTICAL ANALYSIS PLAN FOR

A NON-INTERVENTIONAL, POST-AUTHORIZATION SAFETY STUDY OF PATIENTS WITH RELAPSED OR REFRACTORY MANTLE CELL LYMPHOMA TO FURTHER INVESTIGATE AND CHARACTERIZE THE ASSOCIATION OF LENALIDOMIDE WITH TUMOR FLARE REACTION AND HIGH TUMOR BURDEN

PROTOCOL CC-5013-MCL-005

VERSION 2

DATE: 16-SEPTEMBER-2023

This Statistical Analysis Plan contains information that is confidential and proprietary to Bristol-Myers Squibb Company (BMS)

Summary of key changes				
Version Number	**Effective Date**	**Author**	**Section Number**	**Modification Details**
2	12 Sept 2023	[redacted]	3.4.4.2.4	Inclusion of imputation rule for incomplete lenalidomide dose end date
2	10 Oct 2023	[redacted]	3.4.4.2.3	Inclusion of implementation rule for partial dates for baseline characteristics
2	13 Nov 2023	[redacted]	3.4.4.2.5	Inclusion of imputation rule for missing death date

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1. INTRODUCTION

This statistical analysis plan (SAP) describes the analyses and data presentations for BMS's protocol CC-5013-MCL-005 Amendment 2 (Version 5.0) also known as CA078-P33 "A Non-interventional, Post-authorization Safety Study of Patients with Relapsed or Refractory Mantle Cell Lymphoma (MCL) to Further Investigate and Characterize the Association of Lenalidomide with Tumor Flare Reaction and High Tumor Burden". It contains definitions of analysis populations, derived variables, and statistical methods.

The purpose of the SAP is to ensure the credibility of the study findings by pre-specifying the statistical approaches to the analysis of study data prior to database lock and any data analysis for the final analysis. This SAP will be finalized and signed prior to the clinical database lock for the final analysis. All statistical analyses detailed in this SAP will be conducted using SAS® Version 9.2 or higher.

1.1 Background and Rationale

Lenalidomide is a member of a proprietary series of drugs with immunomodulatory and other properties, referred to as IMiDs®.

In the United States (US), lenalidomide received regulatory approval on 05 Jun 2013, for the treatment of patients with mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib. In the European Union (EU), the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion on 28 Jan 2016 for the use of lenalidomide in the treatment of adult patients with relapsed or refractory mantle cell lymphoma. The European Commission (EC) granted a marketing authorization for this indication on 08 Jul 2016.

While the marketing authorization was granted, the Pharmacovigilance Risk Assessment Committee (PRAC), after reviewing the Risk Management Plan (RMP), requested further assessment of safety issues via post marketing surveillance.

1.2 Research Question

This relapsed or refractory (R/R) MCL PASS will aim to gather additional safety information as a multinational, non-interventional study (NIS) to further investigate the research objectives described in Section 2.

2. OBJECTIVES

This study is designed as a retrospective non-interventional study of patients with R/R MCL to further investigate the following objectives:

2.1 Primary Objective

To quantify and characterize the event of tumor flare reaction (TFR) by tumor burden (assessed based on the last CT scan performed within a maximum of 2 months prior to initiation of administration of lenalidomide) in R/R MCL patients treated with lenalidomide in a real-world setting.

2.2 Secondary Objectives

To quantify and characterize the proportion of early deaths (defined as deaths within 20 weeks of the initial administration of lenalidomide) by tumor burden in R/R MCL patients treated with lenalidomide in a real-world setting.

2.3 Exploratory Objectives

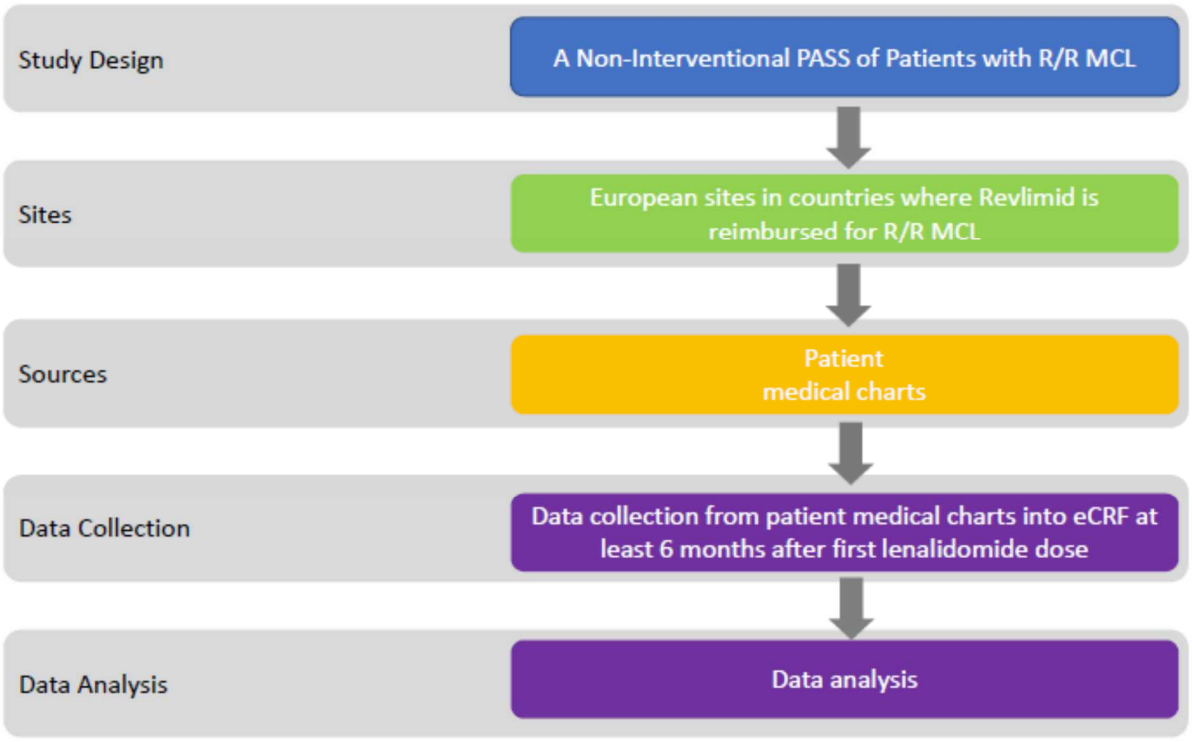
Exploration of factors associated with TFR and with early death will be conducted in multivariate analyses.

3. STUDY DESIGN

3.1 Overview of Study Design

This is a European multinational, retrospective, non-interventional study of patients with R/R MCL. Figure 1 provides a high-level schematic of the design of the study.

Figure 1: Study Design



MCL = mantle cell lymphoma; PASS = post-authorization safety study; R/R = relapsed or refractory; eCRF = electronic case report form.

The study will be performed in Europe. Potential sites will be identified where R/R MCL patients have been treated with lenalidomide and where lenalidomide is reimbursed for this indication. Identification of sites will be done through partnerships such as, but not limited to that with the European Mantle Cell Lymphoma Registry. Other sources including knowledge of, or experience with sites can also be used for site identification purposes. Identified sites will be assessed for feasibility and invited to participate in the study.

3.2 Study Population

The study population will consist of a retrospective cohort of R/R MCL patients who have commenced treatment with lenalidomide after 08 Jul 2016 (date EC marketing authorization was granted).

Inclusion Criteria:

1. Received at least one dose of lenalidomide commencing after 08 Jul 2016 for the treatment of R/R MCL.
2. Informed consent of the patient or an authorized third person or authority, if required by law, given prior to data collection.
3. Patient must be ≥18 years of age.

Exclusion Criteria:

1. Patients will be excluded if they were participating in an interventional clinical trial during the treatment period under observation in this PASS.

3.3 Data Source/Data Collection Process

All data will be collected retrospectively from identified patients. Data from individual patient medical charts will be used as source data. The treating physician or an authorized delegate will enter the data from these medical charts into the web-based eCRF (secondary use of data). A common set of key variables (see Table 2, Table 3 and Table 1) will be collected. Data entry for each enrolled patient will only start at least 6 months after the first dose of lenalidomide. All data will be collected from the first dose of lenalidomide treatment for up to 6 months after the first dose of lenalidomide and including those patients who died within this period.

Table 1: Outcome Variables for Safety

Variables	Data to be Collected
TFR (physician reported)	Adverse Event reported in eCRF/Medical file (onset date, stop date, severity, seriousness, clinical signs and symptoms, lab tests, treatment outcome [treatment discontinuation, dose interruption or dose reduction], relationship to lenalidomide)
TFR symptoms and signs	Painful lymph nodes, painful spleen enlargement, fever[a], rash[a], lymphocytosis[a].
Other AEs	Adverse events related to lenalidomide and not listed in current EU SmPC
Death	Date and cause

AE = adverse event; eCRF = electronic case report form; EU = European Union; SmPC = Summary of Product Characteristics; TFR = tumor flare reaction.
[a] Fever, rash, or lymphocytosis alone do not constitute TFR.

Table 2: Demographics and Clinical Variables

Variables	Data to be Collected
Demographics	
Age	Age (years)
Sex	Female/male
Clinical Variables	
Informed consent	Date of consent

MCL	Date of initial MCL diagnosis; MIPI score at initial diagnosis; Bulky Disease at initial diagnosis; Prior stem cell transplantation (autologous/allogeneic); Date of last relapse/disease progression before lenalidomide therapy; Time from last dose of last therapy before lenalidomide therapy
Medical history	Prior history of TFR; Cardiovascular events (eg, arrhythmia and coronary artery disease); Cerebrovascular events (eg, TIA and stroke); Thromboembolic events (arterial and venous [eg, DVT, PE, and MI]); Peripheral/autonomic neuropathy; Pulmonary, hepatic, renal disease; History of other malignant diseases; Other relevant concomitant diseases or medical conditions
Disease-related characteristics	Tumor burden (high tumor burden is defined as at least one lesion of ≥ 5 cm diameter or at least 3 lesions of ≥3 cm diameter); Bulky disease (≥7 cm) at beginning of lenalidomide treatment; ECOG performance status
Relevant Concomitant Medications related to TFR treatment and/or prophylaxis	Description of Concomitant Medication Indication of Concomitant Medication Start date of Concomitant Medication
Laboratory tests	Hematology: hemoglobin, platelets, WBC, ANC, ALC Biochemistry: LDH, creatinine, creatinine clearance, blood glucose, bilirubin, albumin, ALT, AST, calcium, phosphorus, sodium, potassium, CRP

ALC = absolute lymphocyte count; ALT = alanine aminotransferase; ANC = absolute neutrophil count; AST = aspartate aminotransferase; CRP = C-reactive protein; DVT = deep vein thrombosis; ECOG = Eastern Cooperative Oncology Group; LDH = lactic dehydrogenase; MCL = mantle cell lymphoma; MI = myocardial infarction; MIPI = Mantle Cell Lymphoma International Prognostic Index; PE = pulmonary embolism; TIA = transient ischemic attack; TFR = tumor flare reaction; WBC = white blood cell.

Table 3: Lenalidomide Therapy and Other Treatment Variables

Variables	Data to be Collected
Previous treatments	Number of previous lines of treatment; Description of previous treatments
Lenalidomide treatment	(Date of start and end of treatment [dd/mm/yyyy], lenalidomide dose and regimen, reason for lenalidomide discontinuation or any interruption of therapy with lenalidomide, dose adjustments, where applicable)

3.4 Definition of Study Variables

3.4.1 Outcomes/Endpoints Variables

Outcome variables for safety ("outcomes dataset") are presented in Table 1

Primary Endpoint:

The primary endpoint is the occurrence of tumor flare reaction (TFR) within the date of first administration of lenalidomide and up to 6 months past the date of first administration of lenalidomide.

Secondary Endpoint:

The secondary endpoint is the occurrence of early death event, defined as death within 20 weeks of the initial administration of lenalidomide.

Adverse events related to lenalidomide and not listed in current EU SmPC will also be collected and reported.

3.4.2 Exposure/Independent Variables of Interest

Variables to be evaluated in this study include baseline demographic and clinical variables ("population dataset") (Table 2), treatment variables related to lenalidomide use and other relevant medications ("treatment dataset") (Table 3).

3.4.3 Other Co-Variates/Control Variables

No additional variables

3.4.4 Conventions

3.4.4.1 Handling of Dates

Dates will be stored as numeric variables in the SAS analysis files and reported in DDMMMYYYY format (i.e., the Date9. datetime format in SAS).

Calculation Using Dates

Calculations using dates (e.g., patient's age or relative day after the first dose of lenalidomide) will adhere to the following conventions:

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

Note that lenalidomide treatment Day 1 is the first day of treatment of lenalidomide. Negative study days are reflective of observations obtained prior to the date of the first lenalidomide dose.

- Intervals presented in weeks (e.g. lenalidomide duration) will be transformed from days to weeks by using (without truncation) the following conversion formula:

  WEEKS = DAYS /7

- Intervals presented in months will be transformed from days to months by using (without truncation) the following conversion formula:

  MONTHS = DAYS /30.4375

3.4.4.2 Date Imputation

3.4.4.2.1 Partial Adverse Event Dates / Prior and Concomitant Medication and Procedure

Incomplete Start Date:

Missing day and month

- If the year is the same as the year of the first dosing date, then the day and month of the first dosing date will be assigned to the missing fields.
- If the year is prior to the year of first dosing date, then 31 Dec will be assigned to the missing fields.
- If the year is after the year of first dosing date, then 01 Jan will be assigned to the missing fields.

Missing day only

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

Missing day, month, and year

- The date will not be imputed.

Incomplete Stop Date: If the imputed stop date is before the start date, then the imputed stop date will be set to the start date.

Missing day and month

- If the year of the incomplete stop date is the same as the year of the last dosing date, then the day and month of the last dosing date will be assigned to the missing fields.
- If the year of the incomplete stop date is prior to the year of the last dosing date or prior to the year of the first dosing date, then 31 Dec will be assigned to the missing fields.
- If the year of the incomplete stop date is after the year of the last dosing date, then January 1 will be assigned to the missing fields.

Missing day only

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

3.4.4.2.2 Partial Medical History

Partially missing medical history start dates will be imputed. The 15th of the month will be used to impute a partially missing start date that has only the day missing, and 01 July will be used to impute a partially missing start date that has both the month and day missing.

3.4.4.2.3 Partial Baseline Characteristics

Partially missing Baseline Characteristics dates will be imputed. The 1st of the month will be used to impute a partially missing date that has only the day missing, and 01 January will be used to impute a partially missing date that has both the month and day missing.

3.4.4.2.4 Partial lenalidomide Dose Dates

Incomplete Start Date:

Missing day and month

- No imputation is performed

Missing day only

- The missing day is imputed with the 1st (first) day of the month.

Missing day, month, and year

- No imputation is performed

Incomplete End Date: Partially and completely missing lenalidomide cycle stop dates will be generally imputed with the rule:

lenalidomide cycle stop date = lenalidomide cycle start date + 21 days.

This date will be referred later as the "proposed stop date".

For the "proposed stop date" to be used for imputation, it must be consistent with the following patient's information in the data:

- The patient's next lenalidomide cycle start date.
- The patient's study disposition date.
- The last consistent date induced by the partial stop date, which is defined below.

The next rules will ensure consistency between the imputed lenalidomide cycle stop date and the patient's information in the data:

Missing day and month

- The last consistent date induced by the partial date is the last day of the year (31st Dec).
- The cycle stop date is imputed with the earliest date among the "proposed stop date", the patient's disposition date, the next lenalidomide cycle start date - 1, and the last consistent date.

Missing day only:

- The last consistent date induced by the partial date is the last day of the month.
- The cycle stop date is imputed with the earliest date among the "proposed stop date", the patient's disposition date, the next lenalidomide cycle start date - 1, and the last consistent date.

Missing day, month and year

The cycle stop date will be the earliest date among the "proposed stop date", the patient's disposition date and the next lenalidomide cycle start date - 1.

3.4.4.2.5 Partial death dates:

Missing day, month, and year

- No imputation is performed.

Missing day and month

- If the year of last-known-alive date for the patient is the same as the year of the partial death date, impute the partial death date with the last-known-alive date + 1
- If the year of last-known-alive date for the patient is before the year of the partial death date, impute the partial death date with the 1st of January.

Missing day only

- If the year and month of last-known-alive date for the patient is the same as the year and month of the partial death date, impute the partial death date with the last-known-alive date + 1
- If the year and/or month of the last-known-alive date for the patient is the before the year and/or month of the partial death date, impute the partial death date with the first day of the month.

3.5 Sample size and power

Although the exact number of R/R MCL patients treated with lenalidomide in the European Union (EU) is not known, internal data estimates the number of patients annually who receive second-line therapy in the EU5 region (France, Germany, Italy, Spain and the United Kingdom) as 1,632; and of those, 6% receive lenalidomide alone or in combination with rituximab (Decision Resources Group internal data). Additionally, an estimated 783 patients annually receive third-line therapy, of which 11% are treated with lenalidomide alone or in combination with rituximab. The numbers of patients receiving lenalidomide for additional lines of therapy after third-line would be expected to be very low. Based on these internal estimates, approximately 184 cases per year of R/R MCL patients potentially receive second- or third-line lenalidomide treatment. However, these estimates for treatment with lenalidomide are higher than published real-world data on treatment patterns for R/R MCL (2.3% to 2.7% usage of lenalidomide in second-line treatment, (Visco, 2021; Smith, 2018; Kumar, 2019). Further limitations on the feasibility of recruiting patients include enrolling patients only where lenalidomide is reimbursed, the introduction of new agents for R/R MCL, and a significant number of clinical trials for investigational agents in R/R MCL.

Therefore, based on the above and given that there are no additional patients retrospectively treated with lenalidomide at the active sites, recruitment of a fixed number of 100 patients is considered feasible within the estimated study selection period.

Estimation of the cumulative incidence of TFR

The calculation of precision for the cumulative incidence of TFR is based upon the observed cumulative incidence of TFR (9.6%) in the CC-5013-MCL-002 study of 167 R/R MCL patients treated with lenalidomide with an exact two-sided 95% CI = (5.6%; 15.1%). From the

CC-5013-MCL-002 study, there is a 20% chance that the cumulative incidence of TFR would exceed 12.0% (upper limit of the one-sided 80% CI).

Under the assumption of a true TFR cumulative incidence rate of 9.6%, the precision on the estimate of the TFR cumulative incidence rate with 100 patients is 7.5% (upper limit of the exact two-sided 95% CI).

Under the assumption of a true TFR cumulative incidence rate of 12% in the study population, the precision on the estimate of the TFR cumulative incidence rate with 100 patients is 8.0% (upper limit of the exact two-sided 95% CI).

Estimation of early death rate

In Study CC-5013-MCL-002, 13.2% (22/167) of lenalidomide-treated patients died early. The exact two-sided 95% CI was (8.4%; 19.3%), and there is only a 20% chance that the early death rate would exceed 15.9% (upper limit of the one-sided 80% CI).

With 100 patients, the study will allow a calculation of the early death rate with a precision of +8.2% for the upper limit of the exact two-sided 95% CI if the observed rate is 13.2%, and +8.7% if it is 15.9%.

4. STUDY LIMITATIONS

All AEs (as documented in the medical charts) collected in the study that are related to lenalidomide but not listed in the current EU SmPC will be summarized and frequencies calculated. Since the study is designed with TFR as the main outcome, it may not be sufficiently powered to provide a precise estimate for these adverse events. However, events captured through the review of medical records will be an improvement on spontaneous reporting as these events may not have been captured through normal channels.

Although a multivariate model will be attempted to explore the relationship between TFR and early death, the sample size may not be sufficiently powered, and interpretation of results should be limited to hypothesis generation. There are also limitations to the Kaplan-Meier analysis as the retrospective nature of the study and the secondary use of the data may not provide appropriate granularity in measured time to TFR with regard to the rapid onset of these events.

5. STATISTICAL ANALYSES

The analyses will be descriptive, and no hypotheses will be tested.

Individual patient listings will be provided.

5.1 Description of Study Conduct

Key milestones for the study are:

- Start of data collection: Q1 2019
- Estimated end of data collection: Q4 2023
- Study progress reports:
  - With annual Periodic Safety Update Reports (PSURs)
- Registration in the EU post-authorization study (PAS) register: 03 May 2018
- Final report of study results: Q4 2024

5.2 Description of Study Samples

Two Analysis sets are defined in this study:

Safety Analysis Set (SAS)

Safety Analysis Set (SAS) includes all patients present in the clinical database who received at least one dose of Lenalidomide but not necessarily meet all the inclusion/exclusion criteria.

Per Protocol Analysis Set (PPAS)

The Per Protocol Analysis Set (PPAS) includes patients enrolled in the study who meet all the inclusion/exclusion criteria.

Results will be presented for the Per Protocol Analysis Set. If the Safety Analysis Set contains additional patients, analyses for the primary and secondary endpoints will be repeated on the Safety Analysis Set as sensitivity analysis.

5.2.1 Patient Disposition

The total number of patients enrolled in the study will be summarized.

A summary of subject disposition will be presented for the SAS.

5.2.2 Protocol Deviations/Violations

Protocol deviation will be reported for the SAS.

5.2.3 Demographics, Disease-related Characteristics and Baseline Characteristics

The demographics, disease related characteristics and baseline characteristics will be summarized for the PPAS.

For pre-baseline measures to be considered as of baseline, the windows presented in 4 will be applied.

Table 4: Windows for Inclusion as Baseline Measure

Laboratory measures: chemistry	1 month
Laboratory measures: hematology	1 month
ECOG grade	1 month
Bulky Disease	2 months
Tumor burden	2 months
Baseline history of TFR	2 months
MIPI Score	1 month
B-symptoms presence	2 months
Ann Harbor Stage	2 months
Cyclin D1	2 months

5.2.3.1 Demographics

Patients demographics (age and sex) will be listed and tabulated with appropriate summary statistics.

5.2.3.2 MCL Diagnosis and Disease-related characteristics

The time from initial diagnosis to first dose of lenalidomide will be calculated as (first lenalidomide dose date - date of diagnosis +1) / 30.4375.

The Mantle cell lymphoma International Prognostic Index (MIPI) score, Bulky disease status, B-symptoms presence, Ann Arbor stage and Cyclin D1 detection at initial diagnosis will be tabulated.

5.2.3.3 Baseline characteristics

The time from relapse / disease progression to first dose of lenalidomide and the time from last dose of last therapy to first dose of lenalidomide will also be presented.

The MIPI score, the Eastern Cooperative Oncology Group Performance Status (ECOG), Bulky disease status, B-symptoms presence, Ann Arbor stage, Cyclin D1 detection, history of TFR and High Tumor Burden at baseline will be tabulated.

The proportion of patients with high tumor burden at baseline will be estimated with its two-sided 95% CI. In this study, high tumor burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.

5.2.4 Medical History

Medical and surgical history will be coded using the Medical Dictionary for Drug Regulatory Activities (MedDRA) version 26.0 or later. System organ class and preferred term will be summarized by frequency and percentage. Tables will be provided for patients in the PPAS.

5.2.5 Prior Therapies and Concomitant Medications

All medications including prior therapies and concomitant medications will be coded using the WHODrug Global dictionary terms in the 2023 or the latest version.

Prior Therapies (Including Surgery)

Frequency tabulations of the number of patients with at least one prior therapy, the frequency of the number of prior therapies and type of previous therapies (chemotherapy, immunotherapy, stem cell transplant [separating autologous from allogeneic if possible], radiation, anthracycline/mitoxantrone or cyclophosphamide or rituximab or bortezomib-containing regimens, etc.) will be provided for the PPAS.

Concomitant Medications

Concomitant medications are defined as medications that were either initiated before the first lenalidomide dose date and continued during the lenalidomide treatment or initiated on/after the first lenalidomide dose date and strictly before the date of treatment discontinuation.

A summary showing the number and percentage of patients who took concomitant medications will be presented by WHO therapeutic drug class and generic drug name for the PPAS.

5.2.6 Clinical Laboratory Evaluations

If sufficient data are available, the following results will be tabulated.

Clinical laboratory values at baseline will be presented by summary statistics (n, mean, standard deviation, median, minimum, and maximum) for the PPAS.

If data are available the following clinical laboratory evaluations will be tabulated: hemoglobin, platelets, WBC, ANC, ALC, LDH, creatinine, creatinine clearance, blood glucose, bilirubin, albumin, ALT, AST, calcium, phosphorus, sodium, potassium, CRP.

5.2.7 Lenalidomide Treatment and Extent of Exposure

Lenalidomide treatment duration will be provided based on the PPAS. Descriptive statistics will be provided for treatment duration.

The lenalidomide duration (weeks) is defined as:

[(lenalidomide stop date) – (first lenalidomide start date) + 1]/7.

For patients who are still on lenalidomide at the time of study closure or analysis time, the clinical cutoff date will be used as the lenalidomide end date.

Cumulative dose, defined as the sum of all doses taken across the treatment period in mg will be tabulated.

5.2.8 Efficacy Analysis

No efficacy analysis will be performed.

If sufficient data are available, the best response achieved will be tabulated by frequency for the PPAS.

5.2.9 Safety Analysis

5.2.9.1 Primary Safety Analysis

The frequency of TFR will be reported in summary tables for the PPAS.

Tumor flare reaction will be characterized by clinical assessments and laboratory tests, and tabulated by frequency, severity, seriousness, tumor burden, time to onset, treatment outcome (treatment discontinuation, dose interruption or dose reduction), time to resolution, and relationship to lenalidomide.

If data are available, the TFR will be presented by symptoms and signs (Painful lymph nodes, painful spleen enlargement, fever, rash, lymphocytosis)

Death will be summarized as the frequency of patients who experienced death, and as primary cause of death. Early death will be summarized as the frequency of patients who experienced early death (defined as any death occurring within 20 weeks of the initial administration of lenalidomide), and as primary cause of early death.

5.2.9.2 Analysis of Other Adverse Events

Only treatment emergent adverse events (TEAE) related to lenalidomide that have not been reported in the current Revlimid EU Summary of Product Characteristics (SmPC) will be reported in this study. TEAEs in the document thereafter are referred to as such.

All TEAEs will be coded using MedDRA version 26.0 or later. A treatment related TEAE is defined as TEAE which was considered to be related to the lenalidomide treatment by the investigator.

If a patient experiences the same TEAE more than once with different toxicity grades, the event with the highest grade will be tabulated in "by grade" tables.

If a patient experience multiple TEAEs under the same PT (SOC), then the patient will be counted only once for that PT (SOC).

The incidence of TEAEs related to lenalidomide will be summarized by MedDRA SOC and PT. The intensity of TEAEs will be graded 1 to 5 according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.

Due to the observational nature of the study, missing data may be frequent for grading, relationship of the AE.

If the Safety Analysis Set contains additional patients, analyses of TEAEs will be repeated on the Safety Analysis Set as sensitivity analysis.

5.3 General Methods

- Unless specified otherwise, confidence intervals will be presented as 2-sided at the 95% level.
- Summary statistics will consist of the number and percentage of in each category for discrete variables, and the sample size, minimum, maximum, median, mean and standard deviation for continuous variables.
- All mean and median values will be formatted to one more decimal place than the measured value. Standard deviation values will be formatted to two more decimal places than the measured value.
- All percentages will be rounded to one decimal place. The number and percentage of responses will be presented in the form "XX (XX.x%)", where the percentage is in parentheses.
- All listings will be sorted for presentation in order of country, patient, and date of procedure or event.
- All analysis and summary tables will include the size of the analysis set (i.e., number of patients in the analysis set).

- Adverse event tables will be sorted in frequency descending order by system organ class (SOC), and then within the SOC in frequency descending order by preferred term (PT) on the overall column.
- The day of the first dose of lenalidomide after the diagnosis of R/R MCL will be defined as Day 1.
- Baseline date is defined as the date of first dose of lenalidomide (Day 1).
- Baseline value is defined as the last value on or within a specific time window before the baseline date. If multiple values are present for the same date, the average of these values will be used as the baseline, except otherwise specified in the following sections.
- Patient's age in the inclusion criteria is the age at ICF signing, or, if not available, the age at the first dose of lenalidomide. The baseline age is that at the baseline date.
- If there were multiple post-treatment laboratory measures of the same type from one patient, the mean will be used in the analysis.

5.4 Primary Objective

The anlyses for the primary objective will be performed primarily on the Per Protocol Analysis Set (PPAS) and on the Safety Analysis Set (SAS) for sensitivity analysis, if the two sets are different. If sufficient data are available, the analyses will also be stratified according to the tumor burden at baseline (low vs high tumor burden at baseline).

The primary objective of the study will be estimated by the cumulative incidence (and exact two-sided 95% CI) of tumor flare reaction (TFR) that occurs within the date of first dose of lenalidomide and up to 6 months past the date of first dose of lenalidomide. The cumulative incidence will be calculated as the ratio:

$$\frac{\#\ of\ Patients\ with\ at\ least\ 1\ TFR\ event}{\#\ of\ Patients\ in\ the\ Analysis\ Set}$$

In addition, the Incidence Rate of TFR per 100 Person-Years (with 95% CIs) will be calculated as the ratio:

$$\frac{\#\ of\ Patients\ with\ at\ least\ 1\ TFR\ event}{Total\ Person\ Years} \cdot 100$$

The total Person-Years will be defined as the total time from the first lenalidomide dose date to the first date of TFR for patients reporting TFR. For patients reporting no TFR event during the 6-month period following the first lenalidomide dose the following censoring rules apply:

- Any patient for whom information may exist in the source database after the 6-month period following the first lenalidomide dose will be censored at 6 months.
- Any patient for whom no information exists in the source database at the end of the 6-month study period will be censored at the date of the last information available in the 6-month period.

The 95% CI for the Incidence Rate (IR) per 100 Person-Years will be calculated using the delta method:

$$\text{IR} * \exp\{\pm 1.96 \,/\, \text{square root of n}\}$$

where n is the number of events observed.

If sufficient data are available, the number of TFR event per patient will be tabulated.

Time to TFR will be also analyzed using the Kaplan-Meier (KM) method. Since data are collected retrospectively, the number of time-points each patient may have will be unknown a priori. Given that the precision of the KM method varies with the number of time points available for analysis and that TFR is likely to occur early in treatment with lenalidomide (time to TFR is less than 5 days for almost 25% of patients experiencing TFR and the interquartile range for time to TFR in Study MCL-002 was [0.7, 2.4] weeks (Trněný, 2016), there will likely be an impact on the precision of the estimate using this method.

Consequently, KM analyses will not be performed as primary but as complementary analyses. KM curves will be provided for time to first TFR event. For KM analyses, the same censoring rules as the censoring rules applied to compute the Incidence Rates will be used. Death related to a TFR event will be considered as an event. Death unrelated to TFR will be considered as a censoring event for the Kaplan Meier analysis.

5.5 Secondary Objectives

The anlyses for the secondary objective will be performed primarily on the Per Protocol Analysis Set (PPAS) and on the Safety Analysis Set (SAS) for sensitivity analysis, if the two sets are different. If sufficient data are available, all analyses will also be stratified according to the tumor burden at baseline (low vs high tumor burden at baseline).

The secondary endpoint will be estimated by the cumulative incidence of early death, defined as any death occurring within 20 weeks from the first dose of lenalidomide. The exact two-sided 95% CIs will be calculated. The cumulative incidence of early death will be calculated as the ratio:

$$\frac{\#\ of\ Patients\ with\ Early\ Death}{\#\ of\ Patients\ in\ the\ Analysis\ Set}$$

Time to early death will also be analyzed using the Kaplan-Meier (KM) method. KM curves will be provided for time to early death. For patients with no death reported within 20 weeks after the first dose of lenalidomide, the following censoring rules will be used:

- Any patient for whom information may exist in the source database after the 20-week period following the first lenalidomide dose will be censored at 20 weeks.
- Any patient for whom no information exists in the source database at the end of the 20-week period will be censored at the date of the last information available in the 20-week period.

5.6 Exploratory Objectives

5.6.1 Exploration of Risk Factors associated with TFR

If there is a sufficient number of TFR events (≥ 5 events), exploration of factors associated with TFR will be conducted in multivariable analyses procedure using Cox models to fit time-to-event data. Factors for consideration may include:

- Age, Sex
- Country, site
- History of TFR (yes or no) at baseline
- Tumor burden at baseline (last available information prior to lenalidomide 1st dose).
- Bulky Disease at baseline
- ECOG performance status at baseline

Other risk factor or suspected risk factor for TFR may be added.

The procedure will be performed by first screening all baseline risk factors in a univariate setting. Those risk factors that demonstrate a statistically significant association with the outcome at 0.20 level ($p < 0.20$) will be included in the multiple regression model. The final model will be determined on the complete dataset using a backward elimination variable-selection procedure with $p > 0.10$ as the significance criterion for elimination.

The estimated Hazard Ratios with 95% confidence intervals and p-values will be presented for the univariate regressions and for the risk factors retained in the final multivariate model.

5.6.2 Exploration of Risk Factors associated with early death

If there is a sufficient number of early death events (≥ 5 events), exploration of factors associated with early death will be conducted in multivariate procedure using Cox models to fit time-to-event data. Factors to be included in the models are:

- Age, Sex
- Country, site
- History of TFR (yes or no) at baseline
- Tumor burden at baseline (last available information prior to lenalidomide 1st dose).
- Bulky Disease at baseline
- ECOG performance status at baseline

Other risk factor or suspected risk factor for early death may be added.

The analysis will be performed by first screening all baseline risk factors in a univariate setting. Those risk factors that demonstrate a statistically significant association with the outcome at 0.20 level ($p < 0.20$) will be included in the multiple regression model. The final model will be determined on the complete dataset using a backward elimination variable-selection procedure with $p > 0.10$ as the significance criterion for elimination.

The estimated Hazard Ratios with 95% confidence intervals and p-values will be presented for the univariate regressions and for the risk factors retained in the final multivariate model.

5.7 Interim Analysis

Interim analyses may be conducted if medical need arises.

Study progresses will be report by Annual Periodic Safety Update Reports (PSURs). Only a selected set of outputs will be produced.

The final analysis will be performed at the end of the study.

6. REFERENCES

Sant M, Allemani C, Tereanu C, De Angelis R, Capocaccia R, Visser O, et al. (2010) Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. *Blood.* 116(19):3724-34.

Trněný M, Lamy T, Walewski J, Belada D, Mayer J, Radford J, et al. (2016) Lenalidomide versus investigator's choice in relapsed or refractory mantle cell lymphoma (MCL-002; SPRINT): a Phase 2, randomised, multicentre trial. *Lancet Oncol.* 17(3):319-31.

APPENDIX 1.6 Statistical Tables

364 page(s) excluding cover page

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APPENDIX 1.6 Statistical Tables

- Statistical Tables

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Table 14.1.1
Summary of Reasons for not Enrolling Screened Patients
All Screened Patients

Parameter	Total (N=105) n (%)
Number of Patients Screened	105 (100.0)
Number of Patients Screened but not included in PPAS	4 (3.8)
Reason for Not Enrolling [a]	
Failure to Meet Eligibility Inclusion Criteria	3 (2.9)
INC 1: Received at least one dose of lenalidomide commencing after 08 Jul 2016 for the treatment of R/R MCL	3 (2.9)
INC 2: Informed consent of the patient or an authorised third person or authority, if required by law, given prior to data collection	0 (0.0)
INC 3: Patient >=18 years of age	0 (0.0)
Meet Eligibility Exclusion Criteria	1 (1.0)
EXC 1: Patients were excluded if they were participating in an interventional clinical trial during the treatment period under observation in this PASS	1 (1.0)

EXC=Exclusion; INC=Inclusion; MCL=Mantle Cell Lymphoma; PASS=Post-Authorisation Safety Study; PPAS=Per Protocol Analysis Set; R/R=Relapsed/Refractory.
Enrolled: All patients meeting the eligibility criteria.
[a] Patients may deviate from one or more inclusion/exclusion criteria.
Cross-reference: Listing 16.2.1.2: Patient Discontinued (Including Screen Failure) (All Screened Patients).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a101_t_14_1_1.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 04APR2024 15:53
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Table 14.1.2
Analysis Populations
All Screened Patients

Population	Total (N=105) n (%)
Safety Analysis Set (SAS) [a]	103 (98.1)
Per Protocol Analysis Set (PPAS) [b]	101 (96.2)

Percentages are based upon the number of screened patients.
[a] The Safety Analysis Set (SAS) includes all patients present in the clinical database who received at least one dose of Lenalidomide but not necessarily meet all the inclusion/exclusion criteria. One subject was excluded due to meeting exclusion criteria 01, as detailed in Table 14.1.1. Another subject also failed to meet inclusion criteria 01, which is addressed in the same table. Additionally, neither subject received the study treatment.
[b] The Per Protocol Analysis Set (PPAS) includes patients enrolled in the study who meet all the inclusion/exclusion criteria.
Cross-reference: Listing 16.2.1.3: Study Analysis Populations (Enrolled Patients).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a102_t_14_1_2.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 15MAY2024 16:41
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Table 14.1.3.1
Patients Disposition
Per Protocol Analysis Set

Parameter	Total (N=101) n (%)
Patients who Completed the Study	71 (70.3)
Screen Failures	0 (0.0)
Patients who Discontinued the Study	30 (29.7)
Reason for study discontinuation [a]	
Death	26 (25.7)
Lost to follow-up	4 (4.0)

[a] Percentages are calculated using the SAS.
Cross-reference:
Listing 16.2.1.1: Patients Disposition (All Screened Patients).
Listing 16.2.1.2: Patients Discontinued (Including Screen Failure) (All Screened Patients).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a103_t_14_1_3_1.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 15MAY2024 12:32
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Table 14.1.3.2
Patients Disposition
Safety Analysis Set

Parameter	Total (N=103) n (%)
Patients who Completed the Study	71 (68.9)
Screen Failures	2 (1.9)
Patients who Discontinued the Study	30 (29.1)
Reason for study discontinuation [a]	
Death	26 (25.2)
Lost to follow-up	4 (3.9)

[a] Percentages are calculated using the SAS.
Cross-reference:
Listing 16.2.1.1: Patients Disposition (All Screened Patients).
Listing 16.2.1.2: Patients Discontinued (Including Screen Failure) (All Screened Patients).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a103_t_14_1_3_2.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 15MAY2024 12:15
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Table 14.1.4
Demographics
Per Protocol Analysis Set

Parameter	Total (N=101)
Sex, n (%)	
n (%)	101 (100.0)
Male	80 (79.2)
Female	21 (20.8)
Missing, n (%)	0 (0.0)
Age (years)	
n (missing)	101 (0)
Mean	73.4
SD	8.83
Median	74.0
Q1, Q3	68.0, 80.0
Min, Max	44, 91

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
Percentages are calculated using the number of patients with available (non-missing) data.
Cross-reference: Listing 16.2.4.2.1: Demographics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a104_t_14_1_4.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 31MAY2024 12:18
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.1.4
Demographics
Per Protocol Analysis Set

Parameter	Total (N=101)
Age Categories (years), n (%)	
n (%)	101 (100.0)
<65	15 (14.9)
>=65	86 (85.1)
Missing, n (%)	0 (0.0)
n (%)	101 (100.0)
<75	52 (51.5)
>=75	49 (48.5)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
Percentages are calculated using the number of patients with available (non-missing) data.
Cross-reference: Listing 16.2.4.2.1: Demographics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a104_t_14_1_4.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 31MAY2024 12:18
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Table 14.1.5
Disease-Related Characteristics at the Time of MCL Diagnosis
Per Protocol Analysis Set

Parameter	Total (N=101)
Time from Initial MCL Diagnosis to Start of Lenalidomide (months) [a]	
n (missing)	101 (0)
Mean	66.1
SD	46.03
Median	51.0
Q1, Q3	35.5, 87.4
Min, Max	2, 207
MIPI Score at Diagnosis, n (%)	
n (%)	101 (100.0)
Low Risk	9 (8.9)
Intermediate Risk	18 (17.8)
High Risk	32 (31.7)
Unknown [b]	42 (41.6)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; MCL=Mantle Cell Lymphoma; MIPI=Mantle Cell Lymphoma International Prognostic Index.
Percentages are calculated using the number of patients with available (non-missing) data.
[a] Time from initial MCL diagnosis to start of lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of initial MCL diagnosis + 1) /30.4375].
[b] Unknown = the assessment was done, but the result is not known.
Cross-reference: Listing 16.2.4.1: MCL Diagnosis and Disease-related characteristics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a105_t_14_1_5.sas
Data Source: ADSL Data Extract: Date 20Feb2024 RunTime: 02MAY2024 20:30
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.1.5
Disease-Related Characteristics at the Time of MCL Diagnosis
Per Protocol Analysis Set

Parameter	Total (N=101)
Bulky Disease at Diagnosis, n (%)	
n (%)	101 (100.0)
Yes	11 (10.9)
No	65 (64.4)
Unknown [b]	25 (24.8)
Missing, n (%)	0 (0.0)
B-Symptoms Presence at Diagnosis, n (%)	
n (%)	101 (100.0)
Yes	26 (25.7)
No	53 (52.5)
Unknown [b]	22 (21.8)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; MCL=Mantle Cell Lymphoma; MIPI=Mantle Cell Lymphoma International Prognostic Index.
Percentages are calculated using the number of patients with available (non-missing) data.
[a] Time from initial MCL diagnosis to start of lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of initial MCL diagnosis + 1) /30.4375].
[b] Unknown = the assessment was done, but the result is not known.
Cross-reference: Listing 16.2.4.1: MCL Diagnosis and Disease-related characteristics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a105_t_14_1_5.sas
Data Source: ADSL Data Extract: Date 20Feb2024 RunTime: 02MAY2024 20:30
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.1.5
Disease-Related Characteristics at the Time of MCL Diagnosis
Per Protocol Analysis Set

Parameter	Total (N=101)
t (14; 18), n (%)	
n (%)	97 (96.0)
Positive	12 (12.4)
Negative	17 (17.5)
Indeterminate	68 (70.1)
Missing, n (%)	4 (4.0)
Ann Arbor Stage, n (%)	
n (%)	101 (100.0)
Stage I	2 (2.0)
Stage II	0 (0.0)
Stage III	7 (6.9)
Stage IV	80 (79.2)
Unknown [b]	12 (11.9)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; MCL=Mantle Cell Lymphoma; MIPI=Mantle Cell Lymphoma International Prognostic Index.
Percentages are calculated using the number of patients with available (non-missing) data.
[a] Time from initial MCL diagnosis to start of lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of initial MCL diagnosis + 1) /30.4375].
[b] Unknown = the assessment was done, but the result is not known.
Cross-reference: Listing 16.2.4.1: MCL Diagnosis and Disease-related characteristics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a105_t_14_1_5.sas
Data Source: ADSL Data Extract: Date 20Feb2024 RunTime: 02MAY2024 20:30
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Table 14.1.5
Disease-Related Characteristics at the Time of MCL Diagnosis
Per Protocol Analysis Set

Parameter	Total (N=101)
Cyclin D1, n (%)	
n (%)	101 (100.0)
Positive	65 (64.4)
Negative	9 (8.9)
Indeterminate	27 (26.7)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; MCL=Mantle Cell Lymphoma; MIPI=Mantle Cell Lymphoma International Prognostic Index.
Percentages are calculated using the number of patients with available (non-missing) data.
[a] Time from initial MCL diagnosis to start of lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of initial MCL diagnosis + 1) /30.4375].
[b] Unknown = the assessment was done, but the result is not known.
Cross-reference: Listing 16.2.4.1: MCL Diagnosis and Disease-related characteristics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a105_t_14_1_5.sas
Data Source: ADSL Data Extract: Date 20Feb2024 RunTime: 02MAY2024 20:30
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.1.6
Baseline Characteristics
Per Protocol Analysis Set

Parameter	Total (N=101)
Relapse or refractory MCL, n (%)	
n (%)	101 (100.0)
Yes	101 (100.0)
No	0 (0.0)
Missing, n (%)	0 (0.0)
Time from Relapse/Progression to Start of Lenalidomide (months) [a]	
n (missing)	95 (6)
Mean	4.13
SD	13.395
Median	0.85
Q1, Q3	0.30, 2.23
Min, Max	0.0, 114.3

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; MCL=Mantle Cell Lymphoma; MIPI = Mantle Cell Lymphoma International Prognostic Index; ECOG = Eastern Cooperative Oncology Group
Percentages are calculated using the number of patients with available (non-missing) data.
[a] Time Relapse/Progression to Start of Lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of Relapse/Progression + 1)/30.4375].
[b] Time from Last Dose of Last Therapy to Start of Lenalidomide is calculated as [(Date of last dose of last therapy - Date of 1st dose of lenalidomide + 1)/30.4375].
[c] High tumour burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.
For pre-baseline measures to be considered as of baseline, the measure must fall in a specific time window prior to the Date of 1st dose of lenalidomide. Time windows for all variables at baseline are specified in the SAP.
Cross-reference: Listing 16.2.4.2.2: Baseline Characteristics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a106_t_14_1_6.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 04APR2024 20:39
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Table 14.1.6
Baseline Characteristics
Per Protocol Analysis Set

Parameter	Total (N=101)
Time from Last Dose of Last Therapy to Start of Lenalidomide (months) [b]	
n (missing)	92 (9)
Mean	11.73
SD	21.533
Median	2.10
Q1, Q3	0.64, 11.07
Min, Max	0.0, 113.4

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; MCL=Mantle Cell Lymphoma; MIPI = Mantle Cell Lymphoma International Prognostic Index; ECOG = Eastern Cooperative Oncology Group
Percentages are calculated using the number of patients with available (non-missing) data.
[a] Time Relapse/Progression to Start of Lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of Relapse/Progression + 1)/30.4375].
[b] Time from Last Dose of Last Therapy to Start of Lenalidomide is calculated as [(Date of last dose of last therapy - Date of 1st dose of lenalidomide + 1)/30.4375].
[c] High tumour burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.
For pre-baseline measures to be considered as of baseline, the measure must fall in a specific time window prior to the Date of 1st dose of lenalidomide. Time windows for all variables at baseline are specified in the SAP.
Cross-reference: Listing 16.2.4.2.2: Baseline Characteristics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a106_t_14_1_6.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 04APR2024 20:39
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Table 14.1.6
Baseline Characteristics
Per Protocol Analysis Set

Parameter	Total (N=101)
MIPI Score at Baseline, n (%)	
n (%)	101 (100.0)
Low Risk	8 (7.9)
Intermediate Risk	8 (7.9)
High Risk	21 (20.8)
Unknown	64 (63.4)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; MCL=Mantle Cell Lymphoma; MIPI = Mantle Cell Lymphoma International Prognostic Index; ECOG = Eastern Cooperative Oncology Group
Percentages are calculated using the number of patients with available (non-missing) data.
[a] Time Relapse/Progression to Start of Lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of Relapse/Progression + 1)/30.4375].
[b] Time from Last Dose of Last Therapy to Start of Lenalidomide is calculated as [(Date of last dose of last therapy - Date of 1st dose of lenalidomide + 1)/30.4375].
[c] High tumour burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.
For pre-baseline measures to be considered as of baseline, the measure must fall in a specific time window prior to the Date of 1st dose of lenalidomide. Time windows for all variables at baseline are specified in the SAP.
Cross-reference: Listing 16.2.4.2.2: Baseline Characteristics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a106_t_14_1_6.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 04APR2024 20:39
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.1.6
Baseline Characteristics
Per Protocol Analysis Set

Parameter	Total (N=101)
Bulky Disease at Baseline, n (%)	
n (%)	101 (100.0)
Yes	13 (12.9)
No	61 (60.4)
Unknown	27 (26.7)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; MCL=Mantle Cell Lymphoma; MIPI = Mantle Cell Lymphoma International Prognostic Index; ECOG = Eastern Cooperative Oncology Group
Percentages are calculated using the number of patients with available (non-missing) data.
[a] Time Relapse/Progression to Start of Lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of Relapse/Progression + 1)/30.4375].
[b] Time from Last Dose of Last Therapy to Start of Lenalidomide is calculated as [(Date of last dose of last therapy - Date of 1st dose of lenalidomide + 1)/30.4375].
[c] High tumour burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.
For pre-baseline measures to be considered as of baseline, the measure must fall in a specific time window prior to the Date of 1st dose of lenalidomide. Time windows for all variables at baseline are specified in the SAP.
Cross-reference: Listing 16.2.4.2.2: Baseline Characteristics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a106_t_14_1_6.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 04APR2024 20:39
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.1.6
Baseline Characteristics
Per Protocol Analysis Set

Parameter	Total (N=101)
ECOG Performance Status at Baseline, n (%)	
n (%)	62 (61.4)
0	30 (48.4)
1	23 (37.1)
2	7 (11.3)
3	2 (3.2)
4	0 (0.0)
5	0 (0.0)
Unknown	0 (0.0)
Missing, n (%)	39 (38.6)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; MCL=Mantle Cell Lymphoma; MIPI = Mantle Cell Lymphoma International Prognostic Index; ECOG = Eastern Cooperative Oncology Group
Percentages are calculated using the number of patients with available (non-missing) data.
[a] Time Relapse/Progression to Start of Lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of Relapse/Progression + 1)/30.4375].
[b] Time from Last Dose of Last Therapy to Start of Lenalidomide is calculated as [(Date of last dose of last therapy - Date of 1st dose of lenalidomide + 1)/30.4375].
[c] High tumour burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.
For pre-baseline measures to be considered as of baseline, the measure must fall in a specific time window prior to the Date of 1st dose of lenalidomide. Time windows for all variables at baseline are specified in the SAP.
Cross-reference: Listing 16.2.4.2.2: Baseline Characteristics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a106_t_14_1_6.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 04APR2024 20:39
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.1.6
Baseline Characteristics
Per Protocol Analysis Set

Parameter	Total (N=101)
History of Tumour Flare Reaction, n (%)	
n (%)	101 (100.0)
Yes	5 (5.0)
No	96 (95.0)
Unknown	0 (0.0)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; MCL=Mantle Cell Lymphoma; MIPI = Mantle Cell Lymphoma International Prognostic Index; ECOG = Eastern Cooperative Oncology Group
Percentages are calculated using the number of patients with available (non-missing) data.
[a] Time Relapse/Progression to Start of Lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of Relapse/Progression + 1)/30.4375].
[b] Time from Last Dose of Last Therapy to Start of Lenalidomide is calculated as [(Date of last dose of last therapy - Date of 1st dose of lenalidomide + 1)/30.4375].
[c] High tumour burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.
For pre-baseline measures to be considered as of baseline, the measure must fall in a specific time window prior to the Date of 1st dose of lenalidomide. Time windows for all variables at baseline are specified in the SAP.
Cross-reference: Listing 16.2.4.2.2: Baseline Characteristics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a106_t_14_1_6.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 04APR2024 20:39
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Table 14.1.6
Baseline Characteristics
Per Protocol Analysis Set

Parameter	Total (N=101)
High Tumour Burden at Baseline, n (%) [c]	
n (%)	101 (100.0)
Yes	15 (14.9)
No	48 (47.5)
Unknown	38 (37.6)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; MCL=Mantle Cell Lymphoma; MIPI = Mantle Cell Lymphoma International Prognostic Index; ECOG = Eastern Cooperative Oncology Group
Percentages are calculated using the number of patients with available (non-missing) data.
[a] Time Relapse/Progression to Start of Lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of Relapse/Progression + 1)/30.4375].
[b] Time from Last Dose of Last Therapy to Start of Lenalidomide is calculated as [(Date of last dose of last therapy - Date of 1st dose of lenalidomide + 1)/30.4375].
[c] High tumour burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.
For pre-baseline measures to be considered as of baseline, the measure must fall in a specific time window prior to the Date of 1st dose of lenalidomide. Time windows for all variables at baseline are specified in the SAP.
Cross-reference: Listing 16.2.4.2.2: Baseline Characteristics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a106_t_14_1_6.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 04APR2024 20:39
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Table 14.1.6
Baseline Characteristics
Per Protocol Analysis Set

Parameter	Total (N=101)
Proportion of patients with High Tumour Burden at Baseline, n (%)	15 (14.9)
[95% CI]	[8.6 , 23.3]
B-symptoms presence at Baseline, n (%)	
n (%)	101 (100.0)
Yes	8 (7.9)
No	62 (61.4)
Unknown	31 (30.7)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; MCL=Mantle Cell Lymphoma; MIPI = Mantle Cell Lymphoma International Prognostic Index; ECOG = Eastern Cooperative Oncology Group
Percentages are calculated using the number of patients with available (non-missing) data.
[a] Time Relapse/Progression to Start of Lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of Relapse/Progression + 1)/30.4375].
[b] Time from Last Dose of Last Therapy to Start of Lenalidomide is calculated as [(Date of last dose of last therapy - Date of 1st dose of lenalidomide + 1)/30.4375].
[c] High tumour burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.
For pre-baseline measures to be considered as of baseline, the measure must fall in a specific time window prior to the Date of 1st dose of lenalidomide. Time windows for all variables at baseline are specified in the SAP.
Cross-reference: Listing 16.2.4.2.2: Baseline Characteristics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a106_t_14_1_6.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 04APR2024 20:39
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Table 14.1.6
Baseline Characteristics
Per Protocol Analysis Set

Parameter	Total (N=101)
Ann Arbor Stage at Baseline, n (%)	
n (%)	101 (100.0)
Stage I	1 (1.0)
Stage II	4 (4.0)
Stage III	8 (7.9)
Stage IV	45 (44.6)
Unknown	43 (42.6)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; MCL=Mantle Cell Lymphoma; MIPI = Mantle Cell Lymphoma International Prognostic Index; ECOG = Eastern Cooperative Oncology Group
Percentages are calculated using the number of patients with available (non-missing) data.
[a] Time Relapse/Progression to Start of Lenalidomide is calculated as [(Date of 1st dose of lenalidomide - Date of Relapse/Progression + 1)/30.4375].
[b] Time from Last Dose of Last Therapy to Start of Lenalidomide is calculated as [(Date of last dose of last therapy - Date of 1st dose of lenalidomide + 1)/30.4375].
[c] High tumour burden is defined as at least one lesion of 5 cm or greater in diameter, or at least three lesions of 3 cm or greater in diameter.
For pre-baseline measures to be considered as of baseline, the measure must fall in a specific time window prior to the Date of 1st dose of lenalidomide. Time windows for all variables at baseline are specified in the SAP.
Cross-reference: Listing 16.2.4.2.2: Baseline Characteristics (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a106_t_14_1_6.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 04APR2024 20:39
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Table 14.1.7
Protocol Deviations
Per Protocol Analysis Set

Parameter	Total (N=101)
Number of Patients with at Least One Protocol Deviation	13 (12.9)
ICF ISSUES	12 (11.9)
OTHER	3 (3.0)

Patients may have more than one protocol deviation.
Cross-reference: Listing 16.2.2: Protocol Deviations (Per Protocol Analysis Set)
Additional details on protocol deviations and the actions taken can be found in the listing 16.2.2
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a107_t_14_1_7.sas
Data Source: ADSL, ADDV Data Extract Date: 20Feb2024 RunTime: 28MAY2024 12:07
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.1.8.1
Medical History: Prior Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Patients With at Least One Medical History Condition	57 (56.4)
Infections and infestations	17 (16.8)
Pneumonia	3 (3.0)
Abscess oral	1 (1.0)
COVID-19	1 (1.0)
Cystitis	1 (1.0)
Folliculitis	1 (1.0)
Helicobacter infection	1 (1.0)
Hepatitis B	1 (1.0)
Hepatitis C	1 (1.0)
Herpes simplex	1 (1.0)
Herpes zoster	1 (1.0)
Pneumonia pneumococcal	1 (1.0)
Pseudomonal sepsis	1 (1.0)
Renal tuberculosis	1 (1.0)
Septic shock	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a108_t_14_1_8_1.sas
Data Source: ADMH Data Extract Date: 20Feb2024 RunTime: 17MAR2024 15:55
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Table 14.1.8.1
Medical History: Prior Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Strongyloidiasis	1 (1.0)
Tuberculosis	1 (1.0)
Upper respiratory tract infection	1 (1.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	17 (16.8)
Basal cell carcinoma	2 (2.0)
Breast cancer	2 (2.0)
Renal cell carcinoma	2 (2.0)
Uterine leiomyoma	2 (2.0)
Colorectal adenoma	1 (1.0)
Haemangioma	1 (1.0)
Liposarcoma	1 (1.0)
Lung adenocarcinoma	1 (1.0)
Malignant melanoma	1 (1.0)
Non-Hodgkin's lymphoma	1 (1.0)
Prostate cancer	1 (1.0)
Prostatic adenoma	1 (1.0)
Rectal adenocarcinoma	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a108_t_14_1_8_1.sas
Data Source: ADMH Data Extract Date: 20Feb2024 RunTime: 17MAR2024 15:55
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Table 14.1.8.1
Medical History: Prior Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Seminoma	1 (1.0)
Squamous cell carcinoma	1 (1.0)
Squamous cell carcinoma of lung	1 (1.0)
Transitional cell carcinoma	1 (1.0)
Urethral cancer	1 (1.0)
Cardiac disorders	13 (12.9)
Atrial fibrillation	4 (4.0)
Acute myocardial infarction	3 (3.0)
Atrioventricular block	2 (2.0)
Aortic valve incompetence	1 (1.0)
Atrioventricular block complete	1 (1.0)
Bradycardia	1 (1.0)
Cardiac failure	1 (1.0)
Cardiac flutter	1 (1.0)
Myocardial infarction	1 (1.0)
Myocardial ischaemia	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a108_t_14_1_8_1.sas
Data Source: ADMH Data Extract Date: 20Feb2024 RunTime: 17MAR2024 15:55
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Table 14.1.8.1
Medical History: Prior Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Gastrointestinal disorders	12 (11.9)
Diverticulum	4 (4.0)
Inguinal hernia	3 (3.0)
Anal fistula	1 (1.0)
Dental caries	1 (1.0)
Duodenal ulcer	1 (1.0)
Gastric ulcer	1 (1.0)
Gastrointestinal polyp	1 (1.0)
Haematochezia	1 (1.0)
Umbilical hernia	1 (1.0)
Musculoskeletal and connective tissue disorders	7 (6.9)
Intervertebral disc protrusion	3 (3.0)
Arthritis	1 (1.0)
Osteoarthritis	1 (1.0)
Osteopenia	1 (1.0)
Osteoporosis	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a108_t_14_1_8_1.sas
Data Source: ADMH Data Extract Date: 20Feb2024 RunTime: 17MAR2024 15:55
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.1.8.1
Medical History: Prior Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Renal and urinary disorders	7 (6.9)
Nephrolithiasis	2 (2.0)
Renal colic	2 (2.0)
Renal cyst	1 (1.0)
Renal impairment	1 (1.0)
Urinary bladder polyp	1 (1.0)
Respiratory, thoracic and mediastinal disorders	7 (6.9)
Pleural effusion	3 (3.0)
Pulmonary embolism	2 (2.0)
Acute pulmonary oedema	1 (1.0)
Pneumonitis	1 (1.0)
Pulmonary arterial hypertension	1 (1.0)
Vascular disorders	7 (6.9)
Deep vein thrombosis	3 (3.0)
Hypertension	2 (2.0)
Embolism venous	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a108_t_14_1_8_1.sas
Data Source: ADMH Data Extract Date: 20Feb2024 RunTime: 17MAR2024 15:55
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.1.8.1
Medical History: Prior Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Ischaemia	1 (1.0)
Varicose vein	1 (1.0)
Nervous system disorders	6 (5.9)
Transient ischaemic attack	2 (2.0)
Cerebrovascular accident	1 (1.0)
Gliosis	1 (1.0)
Hemiparesis	1 (1.0)
Paraesthesia	1 (1.0)
Post herpetic neuralgia	1 (1.0)
Syncope	1 (1.0)
Injury, poisoning and procedural complications	5 (5.0)
Accident at work	1 (1.0)
Craniofacial fracture	1 (1.0)
Exposure to communicable disease	1 (1.0)
Femoral neck fracture	1 (1.0)
Joint dislocation	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a108_t_14_1_8_1.sas
Data Source: ADMH Data Extract Date: 20Feb2024 RunTime: 17MAR2024 15:55
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Table 14.1.8.1
Medical History: Prior Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Tibia fracture	1 (1.0)
Hepatobiliary disorders	3 (3.0)
Cholelithiasis	2 (2.0)
Biliary cyst	1 (1.0)
Metabolism and nutrition disorders	3 (3.0)
Dyslipidaemia	2 (2.0)
Diabetes mellitus	1 (1.0)
Hypercholesterolaemia	1 (1.0)
Blood and lymphatic system disorders	2 (2.0)
Neutropenia	1 (1.0)
Thrombocytopenia	1 (1.0)
Endocrine disorders	2 (2.0)
Goitre	1 (1.0)
Hyperthyroidism	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a108_t_14_1_8_1.sas
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Table 14.1.8.1
Medical History: Prior Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Reproductive system and breast disorders	2 (2.0)
Benign prostatic hyperplasia	1 (1.0)
Prostatitis	1 (1.0)
Social circumstances	2 (2.0)
Menopause	1 (1.0)
Tobacco user	1 (1.0)
Congenital, familial and genetic disorders	1 (1.0)
Congenital cystic kidney disease	1 (1.0)
General disorders and administration site conditions	1 (1.0)
Dysplasia	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a108_t_14_1_8_1.sas
Data Source: ADMH Data Extract Date: 20Feb2024 RunTime: 17MAR2024 15:55
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Table 14.1.8.2
Medical History: Concomitant Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Patients With at Least One Medical History Condition	77 (76.2)
Vascular disorders	30 (29.7)
Hypertension	27 (26.7)
Aortic aneurysm	1 (1.0)
Aortic dissection	1 (1.0)
Deep vein thrombosis	1 (1.0)
Peripheral arterial occlusive disease	1 (1.0)
Peripheral venous disease	1 (1.0)
Cardiac disorders	24 (23.8)
Atrial fibrillation	12 (11.9)
Coronary artery disease	5 (5.0)
Ischaemic cardiomyopathy	2 (2.0)
Mitral valve incompetence	2 (2.0)
Myocardial ischaemia	2 (2.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
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Data Source: ADMH Data Extract Date: 20Feb2024 RunTime: 17MAR2024 15:55
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Table 14.1.8.2
Medical History: Concomitant Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Aortic valve incompetence	1 (1.0)
Arrhythmia	1 (1.0)
Atrial flutter	1 (1.0)
Cardiac failure chronic	1 (1.0)
Cardiac failure congestive	1 (1.0)
Left ventricular failure	1 (1.0)
Mitral valve prolapse	1 (1.0)
Pericarditis	1 (1.0)
Supraventricular tachycardia	1 (1.0)
Tricuspid valve incompetence	1 (1.0)
Metabolism and nutrition disorders	22 (21.8)
Dyslipidaemia	7 (6.9)
Type 2 diabetes mellitus	7 (6.9)
Diabetes mellitus	5 (5.0)
Hypercholesterolaemia	4 (4.0)
Hyperlipidaemia	2 (2.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
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Data Source: ADMH Data Extract Date: 20Feb2024 RunTime: 17MAR2024 15:55
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Table 14.1.8.2
Medical History: Concomitant Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Hyperuricaemia	2 (2.0)
Steroid diabetes	1 (1.0)
Type 1 diabetes mellitus	1 (1.0)
Vitamin B12 deficiency	1 (1.0)
Vitamin D deficiency	1 (1.0)
Respiratory, thoracic and mediastinal disorders	17 (16.8)
Chronic obstructive pulmonary disease	7 (6.9)
Obstructive sleep apnoea syndrome	2 (2.0)
Sleep apnoea syndrome	2 (2.0)
Bronchitis chronic	1 (1.0)
Cough	1 (1.0)
Emphysema	1 (1.0)
Haemoptysis	1 (1.0)
Interstitial lung disease	1 (1.0)
Lung disorder	1 (1.0)
Nasal polyps	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
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Table 14.1.8.2
Medical History: Concomitant Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Pulmonary embolism	1 (1.0)
Pulmonary hypertension	1 (1.0)
Sinus polyp	1 (1.0)
Musculoskeletal and connective tissue disorders	14 (13.9)
Osteoarthritis	7 (6.9)
Osteoporosis	3 (3.0)
Rheumatoid arthritis	2 (2.0)
Spinal stenosis	2 (2.0)
Intervertebral disc disorder	1 (1.0)
Osteolysis	1 (1.0)
Spondyloarthropathy	1 (1.0)
Blood and lymphatic system disorders	10 (9.9)
Anaemia	6 (5.9)
Neutropenia	2 (2.0)
Thrombocytopenia	2 (2.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
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Table 14.1.8.2
Medical History: Concomitant Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Anaemia of malignant disease	1 (1.0)
Aplastic anaemia	1 (1.0)
Haemolytic anaemia	1 (1.0)
Hyperleukocytosis	1 (1.0)
Iron deficiency anaemia	1 (1.0)
Lymphocytosis	1 (1.0)
Pancytopenia	1 (1.0)
Splenomegaly	1 (1.0)
Renal and urinary disorders	9 (8.9)
Chronic kidney disease	5 (5.0)
Focal segmental glomerulosclerosis	1 (1.0)
Nephropathy	1 (1.0)
Renal failure	1 (1.0)
Renal impairment	1 (1.0)
Urinary retention	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
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Table 14.1.8.2
Medical History: Concomitant Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Gastrointestinal disorders	8 (7.9)
Chronic gastritis	1 (1.0)
Diverticulum	1 (1.0)
Gastrooesophageal reflux disease	1 (1.0)
Haemorrhoids	1 (1.0)
Inguinal hernia	1 (1.0)
Oesophagitis	1 (1.0)
Pancreatic cyst	1 (1.0)
Pancreatitis	1 (1.0)
Reproductive system and breast disorders	8 (7.9)
Benign prostatic hyperplasia	7 (6.9)
Gynaecomastia	1 (1.0)
Nervous system disorders	7 (6.9)
Carotid arteriosclerosis	1 (1.0)
Carotid artery stenosis	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
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Table 14.1.8.2
Medical History: Concomitant Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Hydrocephalus	1 (1.0)
Ischaemic stroke	1 (1.0)
Neuralgia	1 (1.0)
Neuropathy peripheral	1 (1.0)
Parkinsonism	1 (1.0)
Eye disorders	6 (5.9)
Glaucoma	4 (4.0)
Strabismus	1 (1.0)
Uveitis	1 (1.0)
Endocrine disorders	5 (5.0)
Hyperthyroidism	2 (2.0)
Autoimmune thyroiditis	1 (1.0)
Goitre	1 (1.0)
Primary hypothyroidism	1 (1.0)
Thyroiditis chronic	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
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Data Source: ADMH Data Extract Date: 20Feb2024 RunTime: 17MAR2024 15:55
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Table 14.1.8.2
Medical History: Concomitant Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	5 (5.0)
Prostate cancer	2 (2.0)
Hodgkin's disease	1 (1.0)
Hypergammaglobulinaemia benign monoclonal	1 (1.0)
Non-Hodgkin's lymphoma unspecified histology indolent	1 (1.0)
Prostatic adenoma	1 (1.0)
Psychiatric disorders	5 (5.0)
Adjustment disorder	1 (1.0)
Anxiety disorder	1 (1.0)
Bipolar disorder	1 (1.0)
Depression	1 (1.0)
Mixed anxiety and depressive disorder	1 (1.0)
Infections and infestations	4 (4.0)
Hepatitis B	2 (2.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
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Data Source: ADMH Data Extract Date: 20Feb2024 RunTime: 17MAR2024 15:55
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Table 14.1.8.2
Medical History: Concomitant Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Chronic sinusitis	1 (1.0)
Urinary tract infection	1 (1.0)
Investigations	4 (4.0)
Blood cholesterol increased	1 (1.0)
Blood pressure measurement	1 (1.0)
Hepatitis B core antibody positive	1 (1.0)
Hepatitis B surface antigen positive	1 (1.0)
Immune system disorders	3 (3.0)
Hypogammaglobulinaemia	2 (2.0)
Food allergy	1 (1.0)
Congenital, familial and genetic disorders	2 (2.0)
Arrhythmogenic right ventricular dysplasia	1 (1.0)
Thalassaemia minor	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a109_t_14_1_8_2.sas
Data Source: ADMH Data Extract Date: 20Feb2024 RunTime: 17MAR2024 15:55
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Table 14.1.8.2
Medical History: Concomitant Condition
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Ear and labyrinth disorders	2 (2.0)
Deafness	1 (1.0)
Tinnitus	1 (1.0)
Hepatobiliary disorders	2 (2.0)
Cholelithiasis	1 (1.0)
Liver disorder	1 (1.0)
Skin and subcutaneous tissue disorders	2 (2.0)
Psoriasis	1 (1.0)
Rosacea	1 (1.0)
General disorders and administration site conditions	1 (1.0)
Asthenia	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.4.4 Medical History: Prior and Concomitant Conditions (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a109_t_14_1_8_2.sas
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Table 14.1.9.1
Prior Anti-Cancer Therapies Summary
Per Protocol Analysis Set

Parameter	Total (N=101) n (%)
Patients with at least one prior systemic therapy [a]	98 (97.0)
Number of previous lines of therapy [b]	
n (%)	101 (100.0)
0	1 (1.0)
1	56 (55.4)
2	29 (28.7)
3	7 (6.9)
4+	8 (7.9)
Unknown	0 (0.0)
Missing, n (%)	0 (0.0)

Percentages are calculated using the number of patients with available (non-missing) data.
[a] Prior Anti-Cancer Therapies as any treatment taken and discontinued prior to the 1st dose of lenalidomide.
[b] Number of lines of therapy which started prior to the 1st dose of lenalidomide.
[c] Best response achieved among prior anti-cancer therapies, that is, any therapy which discontinued prior to the 1st dose of lenalidomide.
Cross-reference: 16.2.4.5.1: Prior Anti-Cancer Therapies (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a110_t_14_1_9_1.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 04APR2024 20:48
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Table 14.1.9.1
Prior Anti-Cancer Therapies Summary
Per Protocol Analysis Set

Parameter	Total (N=101) n (%)
Prior stem cell transplant	
n (%)	101 (100.0)
Yes	25 (24.8)
Autologous	25 (24.8)
Allogeneic	2 (2.0)
Unknown	0 (0.0)
No	76 (75.2)
Unknown	0 (0.0)
Missing, n (%)	0 (0.0)

Percentages are calculated using the number of patients with available (non-missing) data.
[a] Prior Anti-Cancer Therapies as any treatment taken and discontinued prior to the 1st dose of lenalidomide.
[b] Number of lines of therapy which started prior to the 1st dose of lenalidomide.
[c] Best response achieved among prior anti-cancer therapies, that is, any therapy which discontinued prior to the 1st dose of lenalidomide.
Cross-reference: 16.2.4.5.1: Prior Anti-Cancer Therapies (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a110_t_14_1_9_1.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 04APR2024 20:48
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Table 14.1.9.1
Prior Anti-Cancer Therapies Summary
Per Protocol Analysis Set

Parameter	Total (N=101) n (%)
Best response achieved prior to Lenalidomide [c]	
n (%)	98 (97.0)
Complete Response	72 (73.5)
Partial Response	16 (16.3)
Stable Disease	5 (5.1)
Progressive Disease	0 (0.0)
Not Evaluable	0 (0.0)
Unknown	5 (5.1)
Missing, n (%)	3 (3.0)

Percentages are calculated using the number of patients with available (non-missing) data.
[a] Prior Anti-Cancer Therapies as any treatment taken and discontinued prior to the 1st dose of lenalidomide.
[b] Number of lines of therapy which started prior to the 1st dose of lenalidomide.
[c] Best response achieved among prior anti-cancer therapies, that is, any therapy which discontinued prior to the 1st dose of lenalidomide.
Cross-reference: 16.2.4.5.1: Prior Anti-Cancer Therapies (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a110_t_14_1_9_1.sas
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Table 14.1.9.2
Prior Systemic Anti-Cancer Therapies
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101) n (%)
Patients with at least one prior systemic anti-cancer therapy	98 (97.0)
Antineoplastic and immunomodulating agents	98 (97.0)
Rituximab	94 (93.1)
Bendamustine	66 (65.3)
Cyclophosphamide	57 (56.4)
Cytarabine	47 (46.5)
Doxorubicin	47 (46.5)
Ibrutinib	46 (45.5)
Vincristine	37 (36.6)
Vincristine sulfate	20 (19.8)
Cisplatin	19 (18.8)
Bortezomib	16 (15.8)
Etoposide	15 (14.9)

Prior Systemic Anti-Cancer Therapies as any treatment taken and discontinued prior to the 1st dose of lenalidomide. Medication not in the WHO drug dictionary will be classified as 'Not Coded'.
ATC=Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: 16.2.4.5.1: Prior Systemic Anti-Cancer Therapies (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a111_t_14_1_9_2.sas
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Table 14.1.9.2
Prior Systemic Anti-Cancer Therapies
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101) n (%)
Melphalan	11 (10.9)
Chlorambucil	10 (9.9)
Carmustine	9 (8.9)
Oxaliplatin	7 (6.9)
Methotrexate	6 (5.9)
Temsirolimus	5 (5.0)
Carboplatin	4 (4.0)
Methotrexate sodium	4 (4.0)
Gemcitabine	3 (3.0)
Ifosfamide	3 (3.0)
Mitoxantrone	3 (3.0)
Obinutuzumab	3 (3.0)
Venetoclax	3 (3.0)
Acalabrutinib	2 (2.0)
Antineoplastic agents	2 (2.0)

Prior Systemic Anti-Cancer Therapies as any treatment taken and discontinued prior to the 1st dose of lenalidomide. Medication not in the WHO drug dictionary will be classified as 'Not Coded'.
ATC=Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: 16.2.4.5.1: Prior Systemic Anti-Cancer Therapies (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a111_t_14_1_9_2.sas
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Table 14.1.9.2
Prior Systemic Anti-Cancer Therapies
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101) n (%)
Cyclophosphamide;doxorubicin hydrochloride;prednisone;rituximab;vincristine sulfate	2 (2.0)
Doxorubicin hydrochloride	2 (2.0)
Liposomal doxorubicin hydrochloride	2 (2.0)
Atezolizumab	1 (1.0)
Bendamustine;cytarabine;rituximab	1 (1.0)
Cisplatin;cytarabine;etoposide;methylprednisolone	1 (1.0)
Dacarbazine	1 (1.0)
Fludarabine	1 (1.0)
Fotemustine	1 (1.0)
Liposomal doxorubicin	1 (1.0)
Other antineoplastic agents	1 (1.0)
Parsaclisib	1 (1.0)
Systemic hormonal preparations, excl. sex hormones and insulins	64 (63.4)
Dexamethasone	38 (37.6)

Prior Systemic Anti-Cancer Therapies as any treatment taken and discontinued prior to the 1st dose of lenalidomide. Medication not in the WHO drug dictionary will be classified as 'Not Coded'.
ATC=Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: 16.2.4.5.1: Prior Systemic Anti-Cancer Therapies (Per Protocol Analysis Set).
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Table 14.1.9.2
Prior Systemic Anti-Cancer Therapies
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101) n (%)
Prednisone	35 (34.7)
Methylprednisolone	9 (8.9)
Prednisolone	9 (8.9)
Methylprednisolone acetate	1 (1.0)
Methylprednisolone sodium succinate	1 (1.0)
Various	11 (10.9)
Ibritumomab tiuxetan	4 (4.0)
Mesna	2 (2.0)
Platinum	2 (2.0)
Cytosine	1 (1.0)
Placebo	1 (1.0)
Radiotherapy	1 (1.0)
Blood and blood forming organs	1 (1.0)

Prior Systemic Anti-Cancer Therapies as any treatment taken and discontinued prior to the 1st dose of lenalidomide. Medication not in the WHO drug dictionary will be classified as 'Not Coded'.
ATC=Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: 16.2.4.5.1: Prior Systemic Anti-Cancer Therapies (Per Protocol Analysis Set).
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Table 14.1.9.2
Prior Systemic Anti-Cancer Therapies
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101) n (%)
Hematopoietic stem cells nos, autologous	1 (1.0)

Prior Systemic Anti-Cancer Therapies as any treatment taken and discontinued prior to the 1st dose of lenalidomide. Medication not in the WHO drug dictionary will be classified as 'Not Coded'.
ATC=Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: 16.2.4.5.1: Prior Systemic Anti-Cancer Therapies (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a111_t_14_1_9_2.sas
Data Source: ADCM Data Extract Date: 20Feb2024 RunTime: 17MAR2024 15:56
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Table 14.1.10
Concomitant Medications
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101)
Patients with at least one concomitant medication	67 (66.3)
Blood and blood forming organs	49 (48.5)
Acetylsalicylic acid	16 (15.8)
Enoxaparin sodium	5 (5.0)
Acetylsalicylate lysine	4 (4.0)
Apixaban	4 (4.0)
Clopidogrel	3 (3.0)
Folic acid	3 (3.0)
Tinzaparin sodium	3 (3.0)
Calcium folinate	2 (2.0)
Enoxaparin	2 (2.0)
Epoetin alfa	2 (2.0)
Epoetin zeta	2 (2.0)
Nadroparin calcium	2 (2.0)

Concomitant medications are defined as medications other than study medications which are taken at any time on-treatment, i.e. on or after the first day of study treatment and before the date of treatment discontinuation. Medications not in the WHO drug dictionary will be classified as 'Not Coded'.
Medications taken for MCL are excluded.
ATC = Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: Listing 16.2.4.5.2: Concomitant Medications Other than Lenalinomide for MCL (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a112_t_14_1_10.sas
Data Source: ADCM Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:16
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Table 14.1.10
Concomitant Medications
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101)
Ascorbic acid;folic acid;pyridoxine hydrochloride;saccharated iron oxide;vitamin b12 nos	1 (1.0)
Cyanocobalamin	1 (1.0)
Dabigatran	1 (1.0)
Dabigatran etexilate mesilate	1 (1.0)
Darbepoetin alfa	1 (1.0)
Edoxaban	1 (1.0)
Edoxaban tosilate	1 (1.0)
Erythropoietin	1 (1.0)
Ferrous sulfate	1 (1.0)
Fondaparinux	1 (1.0)
Phenprocoumon	1 (1.0)
Rivaroxaban	1 (1.0)
Romiplostim	1 (1.0)
Vitamin b12 nos	1 (1.0)
Antiinfectives for systemic use	40 (39.6)

Concomitant medications are defined as medications other than study medications which are taken at any time on-treatment, i.e. on or after the first day of study treatment and before the date of treatment discontinuation. Medications not in the WHO drug dictionary will be classified as 'Not Coded'.
Medications taken for MCL are excluded.
ATC = Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: Listing 16.2.4.5.2: Concomitant Medications Other than Lenalinomide for MCL (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a112_t_14_1_10.sas
Data Source: ADCM Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:16
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Table 14.1.10
Concomitant Medications
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101)
Sulfamethoxazole;trimethoprim	20 (19.8)
Aciclovir	12 (11.9)
Valaciclovir hydrochloride	6 (5.9)
Lamivudine	5 (5.0)
Levofloxacin	4 (4.0)
Valaciclovir	4 (4.0)
Entecavir	2 (2.0)
Moxifloxacin hydrochloride	2 (2.0)
Trimethoprim	2 (2.0)
Amoxicillin	1 (1.0)
Amoxicillin;clavulanic acid	1 (1.0)
Amphotericin b	1 (1.0)
Azithromycin	1 (1.0)
Cefepime	1 (1.0)
Ceftriaxone	1 (1.0)
Ceftriaxone sodium	1 (1.0)

Concomitant medications are defined as medications other than study medications which are taken at any time on-treatment, i.e. on or after the first day of study treatment and before the date of treatment discontinuation. Medications not in the WHO drug dictionary will be classified as 'Not Coded'.
Medications taken for MCL are excluded.
ATC = Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: Listing 16.2.4.5.2: Concomitant Medications Other than Lenalinomide for MCL (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a112_t_14_1_10.sas
Data Source: ADCM Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:16
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.1.10
Concomitant Medications
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101)
Cilgavimab	1 (1.0)
Ciprofloxacin	1 (1.0)
Clarithromycin	1 (1.0)
Dapsone	1 (1.0)
Fluconazole	1 (1.0)
Immunoglobulin human normal	1 (1.0)
Nystatin	1 (1.0)
Oseltamivir	1 (1.0)
Piperacillin sodium;tazobactam sodium	1 (1.0)
Sulfamethoxazole	1 (1.0)
Sulfametrole;trimethoprim	1 (1.0)
Tixagevimab	1 (1.0)
Alimentary tract and metabolism	38 (37.6)
Omeprazole	14 (13.9)
Colecalciferol	7 (6.9)

Concomitant medications are defined as medications other than study medications which are taken at any time on-treatment, i.e. on or after the first day of study treatment and before the date of treatment discontinuation. Medications not in the WHO drug dictionary will be classified as 'Not Coded'.
Medications taken for MCL are excluded.
ATC = Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: Listing 16.2.4.5.2: Concomitant Medications Other than Lenalinomide for MCL (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a112_t_14_1_10.sas
Data Source: ADCM Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:16
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.1.10
Concomitant Medications
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101)
Lansoprazole	6 (5.9)
Pantoprazole sodium sesquihydrate	6 (5.9)
Metformin	4 (4.0)
Esomeprazole	3 (3.0)
Ondansetron	3 (3.0)
Pantoprazole	3 (3.0)
Magnesium	2 (2.0)
Metoclopramide	2 (2.0)
Metoclopramide hydrochloride	2 (2.0)
Budesonide	1 (1.0)
Calcium carbonate	1 (1.0)
Calcium carbonate;colecalciferol	1 (1.0)
Chlorhexidine	1 (1.0)
Chlorhexidine gluconate	1 (1.0)
Chlorhexidine gluconate;macrogol;saccharin sodium;sodium bicarbonate;sodium edetate	1 (1.0)
Empagliflozin	1 (1.0)

Concomitant medications are defined as medications other than study medications which are taken at any time on-treatment, i.e. on or after the first day of study treatment and before the date of treatment discontinuation. Medications not in the WHO drug dictionary will be classified as 'Not Coded'.
Medications taken for MCL are excluded.
ATC = Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: Listing 16.2.4.5.2: Concomitant Medications Other than Lenalinomide for MCL (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a112_t_14_1_10.sas
Data Source: ADCM Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:16
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.1.10
Concomitant Medications
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101)
Gliclazide	1 (1.0)
Insulin	1 (1.0)
Magaldrate	1 (1.0)
Magnesium;potassium	1 (1.0)
Metformin hydrochloride;sitagliptin phosphate monohydrate	1 (1.0)
Minerals nos	1 (1.0)
Nystatin	1 (1.0)
Omeprazole sodium	1 (1.0)
Potassium	1 (1.0)
Potassium chloride	1 (1.0)
Ranitidine	1 (1.0)
Repaglinide	1 (1.0)
Rifaximin	1 (1.0)
Sodium bicarbonate	1 (1.0)
Ursodeoxycholic acid	1 (1.0)
Vitamin b complex	1 (1.0)

Concomitant medications are defined as medications other than study medications which are taken at any time on-treatment, i.e. on or after the first day of study treatment and before the date of treatment discontinuation. Medications not in the WHO drug dictionary will be classified as 'Not Coded'.
Medications taken for MCL are excluded.
ATC = Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: Listing 16.2.4.5.2: Concomitant Medications Other than Lenalinomide for MCL (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a112_t_14_1_10.sas
Data Source: ADCM Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:16
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Table 14.1.10
Concomitant Medications
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101)
Cardiovascular system	30 (29.7)
Furosemide	8 (7.9)
Bisoprolol fumarate	6 (5.9)
Ramipril	6 (5.9)
Amlodipine	4 (4.0)
Simvastatin	4 (4.0)
Amiodarone hydrochloride	2 (2.0)
Atenolol	2 (2.0)
Bisoprolol	2 (2.0)
Isosorbide mononitrate	2 (2.0)
Nebivolol hydrochloride	2 (2.0)
Torasemide	2 (2.0)
Amlodipine besilate;olmesartan medoxomil	1 (1.0)
Atorvastatin	1 (1.0)
Atorvastatin calcium	1 (1.0)

Concomitant medications are defined as medications other than study medications which are taken at any time on-treatment, i.e. on or after the first day of study treatment and before the date of treatment discontinuation. Medications not in the WHO drug dictionary will be classified as 'Not Coded'.
Medications taken for MCL are excluded.
ATC = Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: Listing 16.2.4.5.2: Concomitant Medications Other than Lenalinomide for MCL (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a112_t_14_1_10.sas
Data Source: ADCM Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:16
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Table 14.1.10
Concomitant Medications
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101)
Candesartan cilexetil	1 (1.0)
Canrenone	1 (1.0)
Doxazosin mesilate	1 (1.0)
Ezetimibe	1 (1.0)
Fluvastatin	1 (1.0)
Hydrochlorothiazide;ramipril	1 (1.0)
Ivabradine	1 (1.0)
Lisinopril	1 (1.0)
Metildigoxin	1 (1.0)
Metoprolol	1 (1.0)
Metoprolol tartrate	1 (1.0)
Olmesartan medoxomil	1 (1.0)
Pitavastatin	1 (1.0)
Rosuvastatin	1 (1.0)
Musculo-skeletal system	20 (19.8)

Concomitant medications are defined as medications other than study medications which are taken at any time on-treatment, i.e. on or after the first day of study treatment and before the date of treatment discontinuation. Medications not in the WHO drug dictionary will be classified as 'Not Coded'.
Medications taken for MCL are excluded.
ATC = Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: Listing 16.2.4.5.2: Concomitant Medications Other than Lenalinomide for MCL (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a112_t_14_1_10.sas
Data Source: ADCM Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:16
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Table 14.1.10
Concomitant Medications
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101)
Allopurinol	17 (16.8)
Febuxostat	4 (4.0)
Ibuprofen	1 (1.0)
Antineoplastic and immunomodulating agents	16 (15.8)
Filgrastim	13 (12.9)
Bicalutamide	1 (1.0)
Granulocyte colony stimulating factor	1 (1.0)
Letrozole	1 (1.0)
Sirolimus	1 (1.0)
Tacrolimus	1 (1.0)
Systemic hormonal preparations, excl. sex hormones and insulins	13 (12.9)
Prednisone	5 (5.0)
Levothyroxine sodium	3 (3.0)
Methylprednisolone	2 (2.0)

Concomitant medications are defined as medications other than study medications which are taken at any time on-treatment, i.e. on or after the first day of study treatment and before the date of treatment discontinuation. Medications not in the WHO drug dictionary will be classified as 'Not Coded'.
Medications taken for MCL are excluded.
ATC = Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: Listing 16.2.4.5.2: Concomitant Medications Other than Lenalinomide for MCL (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a112_t_14_1_10.sas
Data Source: ADCM Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:16
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Table 14.1.10
Concomitant Medications
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101)
Dexamethasone	1 (1.0)
Levothyroxine	1 (1.0)
Methylprednisolone sodium succinate	1 (1.0)
Prednisolone	1 (1.0)
Thiamazole	1 (1.0)
Nervous system	12 (11.9)
Paracetamol	3 (3.0)
Lorazepam	2 (2.0)
Amitriptyline hydrochloride	1 (1.0)
Benserazide hydrochloride;levodopa	1 (1.0)
Escitalopram	1 (1.0)
Fentanyl	1 (1.0)
Hydroxyzine hydrochloride	1 (1.0)
Lamotrigine	1 (1.0)
Lormetazepam	1 (1.0)

Concomitant medications are defined as medications other than study medications which are taken at any time on-treatment, i.e. on or after the first day of study treatment and before the date of treatment discontinuation. Medications not in the WHO drug dictionary will be classified as 'Not Coded'.
Medications taken for MCL are excluded.
ATC = Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: Listing 16.2.4.5.2: Concomitant Medications Other than Lenalinomide for MCL (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a112_t_14_1_10.sas
Data Source: ADCM Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:16
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Table 14.1.10
Concomitant Medications
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101)
Metoprolol	1 (1.0)
Mirtazapine	1 (1.0)
Naloxone hydrochloride;oxycodone hydrochloride	1 (1.0)
Pregabalin	1 (1.0)
Venlafaxine	1 (1.0)
Zolpidem tartrate	1 (1.0)
Genito urinary system and sex hormones	6 (5.9)
Silodosin	3 (3.0)
Alfuzosin hydrochloride	1 (1.0)
Dutasteride	1 (1.0)
Finasteride	1 (1.0)
Tamsulosin	1 (1.0)
Respiratory system	5 (5.0)
Beclometasone	1 (1.0)

Concomitant medications are defined as medications other than study medications which are taken at any time on-treatment, i.e. on or after the first day of study treatment and before the date of treatment discontinuation. Medications not in the WHO drug dictionary will be classified as 'Not Coded'.
Medications taken for MCL are excluded.
ATC = Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: Listing 16.2.4.5.2: Concomitant Medications Other than Lenalinomide for MCL (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a112_t_14_1_10.sas
Data Source: ADCM Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:16
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Table 14.1.10
Concomitant Medications
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101)
Cetirizine	1 (1.0)
Desloratadine	1 (1.0)
Dexchlorpheniramine maleate	1 (1.0)
Ebastine	1 (1.0)
Rupatadine	1 (1.0)
Tiotropium bromide	1 (1.0)
Sensory organs	3 (3.0)
Latanoprost	2 (2.0)
Betamethasone sodium phosphate	1 (1.0)
Brinzolamide	1 (1.0)
Timolol	1 (1.0)
Antiparasitic products, insecticides and repellents	1 (1.0)
Pentamidine	1 (1.0)

Concomitant medications are defined as medications other than study medications which are taken at any time on-treatment, i.e. on or after the first day of study treatment and before the date of treatment discontinuation. Medications not in the WHO drug dictionary will be classified as 'Not Coded'.
Medications taken for MCL are excluded.
ATC = Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: Listing 16.2.4.5.2: Concomitant Medications Other than Lenalinomide for MCL (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a112_t_14_1_10.sas
Data Source: ADCM Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:16
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Table 14.1.10
Concomitant Medications
Per Protocol Analysis Set

ATC1 Dictionary Level Preferred Name [a]	Total (N=101)
Dermatologicals	1 (1.0)
Methylprednisolone	1 (1.0)
Various	1 (1.0)
Rasburicase	1 (1.0)

Concomitant medications are defined as medications other than study medications which are taken at any time on-treatment, i.e. on or after the first day of study treatment and before the date of treatment discontinuation. Medications not in the WHO drug dictionary will be classified as 'Not Coded'.
Medications taken for MCL are excluded.
ATC = Anatomical Therapeutical Chemical (Classification System).
[a] Coded using WHO Drug Version March 2023. A patient with multiple occurrences of a drug class or drug is counted only once in the specific ATC classification or preferred name, respectively.
Cross-reference: Listing 16.2.4.5.2: Concomitant Medications Other than Lenalinomide for MCL (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a112_t_14_1_10.sas
Data Source: ADCM Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:16
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.1
Treatment Exposure
Per Protocol Analysis Set

Parameter	Total (N=101)
Treatment Duration (weeks) [a]	
n (missing)	101 (0)
Mean	17.41
SD	10.086
Median	22.00
Q1, Q3	7.00, 26.14
Min, Max	0.4, 28.4
Cumulative dose (mg) [b]	
n (missing)	101 (0)
Mean	1564.06
SD	1096.915
Median	1340.00
Q1, Q3	570.00, 2430.00
Min, Max	20.0, 3800.0

AE=Adverse Event; Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Defined as (date of last lenalidomide dose - date of first lenalidomide dose + 1)/7 without considering interruptions.
[b] Cumulative dose, defined as the sum of all doses taken across the treatment period in mg.
[c] Other reason specified is described in Table 14.2.1a.
[d] Calculated based on the number of patients with any dose reduction/interruption.
[e] Calculated based on the number of patients with any dose reduction/interruption due to an AE.
Cross-reference: Listing 16.2.5.1: Treatment Exposure (Per Protocol Analysis Set)/Listing 16.2.5.2 Treatment Doses of MCL Therapies (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a113_t_14_2_1.sas
Data Source: ADEXSUM Data Extract Date: 20Feb2024 RunTime: 23AUG2024 10:41
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.1
Treatment Exposure
Per Protocol Analysis Set

Parameter	Total (N=101)
Patients with Lenalidomide dose Reduction/Interruption, n (%)	85 (84.2)
Reason for Dose Reduction/Interruption, n (%)	
Adverse Event	48 (47.5)
Investigator Decision	13 (12.9)
Progressive disease	21 (20.8)
Rest Period	29 (28.7)
Other [c]	22 (21.8)

AE=Adverse Event; Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Defined as (date of last lenalidomide dose - date of first lenalidomide dose + 1)/7 without considering interruptions.
[b] Cumulative dose, defined as the sum of all doses taken across the treatment period in mg.
[c] Other reason specified is described in Table 14.2.1a.
[d] Calculated based on the number of patients with any dose reduction/interruption.
[e] Calculated based on the number of patients with any dose reduction/interruption due to an AE.
Cross-reference: Listing 16.2.5.1: Treatment Exposure (Per Protocol Analysis Set)/Listing 16.2.5.2 Treatment Doses of MCL Therapies (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a113_t_14_2_1.sas
Data Source: ADEXSUM Data Extract Date: 20Feb2024 RunTime: 23AUG2024 10:41
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Table 14.2.1
Treatment Exposure
Per Protocol Analysis Set

Parameter	Total (N=101)
Time to First Dose Reduction/Interruption (days) [d]	
n (missing)	85 (0)
Mean	43.9
SD	40.31
Median	29.0
Q1, Q3	15.0, 57.0
Min, Max	3, 169
Time to First Dose Reduction/Interruption due to an AE (days) [e]	
n (missing)	48 (0)
Mean	47.1
SD	46.25
Median	29.5
Q1, Q3	15.0, 57.0
Min, Max	3, 172

AE=Adverse Event; Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Defined as (date of last lenalidomide dose - date of first lenalidomide dose + 1)/7 without considering interruptions.
[b] Cumulative dose, defined as the sum of all doses taken across the treatment period in mg.
[c] Other reason specified is described in Table 14.2.1a.
[d] Calculated based on the number of patients with any dose reduction/interruption.
[e] Calculated based on the number of patients with any dose reduction/interruption due to an AE.
Cross-reference: Listing 16.2.5.1: Treatment Exposure (Per Protocol Analysis Set)/Listing 16.2.5.2 Treatment Doses of MCL Therapies (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a113_t_14_2_1.sas
Data Source: ADEXSUM Data Extract Date: 20Feb2024 RunTime: 23AUG2024 10:41
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.1a
Other Reason for Dose Reduction/Interruption
Per Protocol Analysis Set

Parameter	Total (N=101)
All events	22 (21.8%)
Department organisation	2 (2.0%)
3rd october is a bank holiday in germany.	1 (1.0%)
Cannot be scheduled before/after due to patient's agenda	1 (1.0%)
Death	1 (1.0%)
Delayed by the patient without specific reason	1 (1.0%)
Finishes chemo and prepares for sister's hla-identical phpt	1 (1.0%)
Hepatic toxicity and new line of treatment started	1 (1.0%)
Logistic issues	1 (1.0%)
Logistical problems	1 (1.0%)
Logistical reason	1 (1.0%)
Not known	1 (1.0%)
Patient decision of a 4 week break interval	1 (1.0%)
Reason not reported	1 (1.0%)
Revlimid was paused at the patient's request	1 (1.0%)
Scheduling conflicts - patient could not visit centre for re-prescription	1 (1.0%)
Skin rash	1 (1.0%)
Staging nach 4 zyklen r2	1 (1.0%)
Subject forgot 1 dose between 11oct2021 and 1nov2021, exact date unknown.	1 (1.0%)

This table illustrates the count of subjects experiencing at least one 'Other' reason for dose reduction or interruption.
The statement 'Staging nach 4 zyklen r2' is entered in German, which means 'Staging after 4 cycles R2' in English.
'Not known' and 'Unknown' convey the same meaning, although sites have entered them differently.
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a113_t_14_2_1a.sas
Data Sourcea: ADEX Data Extract Date: 20Feb2024 RunTime: 21AUG2024 13:15
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.1a
Other Reason for Dose Reduction/Interruption
Per Protocol Analysis Set

Parameter	Total (N=101)
The patient was admitted for fever on 20-28 /may/2019 and after discharge, the first available appointment was on 03/jun/2019.	1 (1.0%)
Therapy shortened, break due to an intervention in dermatology	1 (1.0%)
Unknown	1 (1.0%)

This table illustrates the count of subjects experiencing at least one 'Other' reason for dose reduction or interruption.
The statement 'Staging nach 4 zyklen r2' is entered in German, which means 'Staging after 4 cycles R2' in English.
'Not known' and 'Unknown' convey the same meaning, although sites have entered them differently.
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a113_t_14_2_1a.sas
Data Sourcea: ADEX Data Extract Date: 20Feb2024 RunTime: 21AUG2024 13:15
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.2.1
Incidence of Tumour Flare Reaction (TFR) by Tumour burden status at baseline
Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other [c] (N=38)	Total (N=101)
Number of patients with at least one TFR	1	2	3	6
Cumulative Incidence of TFR %	2.1	13.3	7.9	5.9
[95% CI][a]	(0.1, 11.1)	(1.7, 40.5)	(1.7, 21.4)	(2.2, 12.5)
Incidence Rate of TFR per 100 Person-Years, %	4.7	34.2	20.9	14.4
[95% CI][b]	(0.7, 33.3)	(8.5, 136.6)	(6.7, 64.7)	(6.5, 32.1)

CI = Confidence Interval
[a] Clopper-Pearson is used to calculte 95% CI
[b] 95% CI for IR per 100 person-years is calculated using the method by RG Miller: IR*exp{+/- 1.96/square root of n}.
[c] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Cross-Reference: Listing 16.2.6.1: Tumour Flare Reaction and Survival Status (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a114_t_14_2_2_1.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:37
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.2.2
Incidence of Tumour Flare Reaction (TFR) by Tumour Burden Status at Baseline
Safety Analysis Set

	Low Tumour Burden (N=49)	High Tumour Burden (N=15)	Other [c] (N=39)	Total (N=103)
Number of patients with at least one TFR	1	2	3	6
Cumulative Incidence of TFR %	2.0	13.3	7.7	5.8
[95% CI][a]	(0.1, 10.9)	(1.7, 40.5)	(1.6, 20.9)	(2.2, 12.2)
Incidence Rate of TFR per 100 Person-Years, %	4.6	34.2	20.2	14.2
[95% CI][b]	(0.7, 32.8)	(8.5, 136.6)	(6.5, 62.5)	(6.4, 31.5)

CI = Confidence Interval
[a] Clopper-Pearson is used to calculte 95% CI
[b] 95% CI for IR per 100 person-years is calculated using the method by RG Miller: IR*exp{+/- 1.96/square root of n}.
[c] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a114_t_14_2_2_2.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:38
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.3.1
Summary of Time to Tumour Flare Reaction (TFR) Onset by Tumour Burden Status at Baseline
Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other [e] (N=38)	Total (N=101)
TFR-Free Survival, N				
n (missing)	48 (0)	15 (0)	38 (0)	101 (0)
Censored n (%)	47 (97.9)	13 (86.7)	35 (92.1)	95 (94.1)
Events n (%)	1 (2.1)	2 (13.3)	3 (7.9)	6 (5.9)
Median Time to TFR Onset [a](months)	NR	NR	NR	NR
Two-sided 95% CI [b]	(NR, NR)	(NR, NR)	(NR, NR)	(NR, NR)

CI = Confidence Interval; Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; NC=Not calculable; NR=Not reached.
The time to TFR is defined as (TFR onset date - date of first Lenalidomide dose date + 1)/30.4375. Patients reporting no TFR will be censored at the date of last information available within the 6-month period. Death related to a TFR event will be considered as an event. Death unrelated to TFR will be considered as a censoring event. All times to event will be censored at 6 months after the first Lenalidomide dose date
[a] Median is based on Kaplan-Meier estimates.
[b] Two-sided Confidence interval based on the Kaplan-Meier estimates.
[c] Probability based on Kaplan-Meier estimates.
[d] The mean and median are the univariate statistics without adjusting for censoring.
[e] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
the following warning shows up: 'The likelihood ratio test for strata homogeneity is questionable since some strata have no events'
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a115_t_14_2_3_1.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 15APR2024 9:36
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.3.1
Summary of Time to Tumour Flare Reaction (TFR) Onset by Tumour Burden Status at Baseline
Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other [e] (N=38)	Total (N=101)
Timepoints TFR-Free Survival probability[c]				
28 days (Cycle 1) (95% CI)	97.9 (86.1, 99.7)	93.3 (61.3, 99.0)	94.6 (80.0, 98.6)	96.0 (89.7, 98.5)
56 days (Cycle 2) (95% CI)	97.9 (86.1, 99.7)	93.3 (61.3, 99.0)	94.6 (80.0, 98.6)	96.0 (89.7, 98.5)
84 days (Cycle 3) (95% CI)	97.9 (86.1, 99.7)	93.3 (61.3, 99.0)	94.6 (80.0, 98.6)	96.0 (89.7, 98.5)
6 months estimate (95% CI)	97.9 (86.1, 99.7)	84.8 (51.2, 96.0)	90.9 (74.1, 97.0)	93.4 (85.9, 97.0)

CI = Confidence Interval; Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; NC=Not calculable; NR=Not reached.
The time to TFR is defined as (TFR onset date - date of first Lenalidomide dose date + 1)/30.4375. Patients reporting no TFR will be censored at the date of last information available within the 6-month period. Death related to a TFR event will be considered as an event. Death unrelated to TFR will be considered as a censoring event. All times to event will be censored at 6 months after the first Lenalidomide dose date
[a] Median is based on Kaplan-Meier estimates.
[b] Two-sided Confidence interval based on the Kaplan-Meier estimates.
[c] Probability based on Kaplan-Meier estimates.
[d] The mean and median are the univariate statistics without adjusting for censoring.
[e] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
the following warning shows up: 'The likelihood ratio test for strata homogeneity is questionable since some strata have no events'
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a115_t_14_2_3_1.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 15APR2024 9:36
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.3.1
Summary of Time to Tumour Flare Reaction (TFR) Onset by Tumour Burden Status at Baseline
Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other [e] (N=38)	Total (N=101)
Follow-up Duration (months)				
n	48	15	38	101
Mean [d]	5.33	4.68	4.54	4.94
SD	1.554	2.285	2.008	1.871
Median [d]	6.03	6.01	6.02	6.03
Q1, Q3	5.95, 6.03	2.66, 6.03	3.02, 6.03	4.24, 6.03
Min, Max	0.33, 6.03	0.26, 6.03	0.16, 6.03	0.16, 6.03

CI = Confidence Interval; Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; NC=Not calculable; NR=Not reached.
The time to TFR is defined as (TFR onset date - date of first Lenalidomide dose date + 1)/30.4375. Patients reporting no TFR will be censored at the date of last information available within the 6-month period. Death related to a TFR event will be considered as an event. Death unrelated to TFR will be considered as a censoring event. All times to event will be censored at 6 months after the first Lenalidomide dose date
[a] Median is based on Kaplan-Meier estimates.
[b] Two-sided Confidence interval based on the Kaplan-Meier estimates.
[c] Probability based on Kaplan-Meier estimates.
[d] The mean and median are the univariate statistics without adjusting for censoring.
[e] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
the following warning shows up: 'The likelihood ratio test for strata homogeneity is questionable since some strata have no events'
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a115_t_14_2_3_1.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 15APR2024 9:36
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.3.2
Summary of Time to Tumour Flare Reaction (TFR) Onset by Tumour Burden Status at Baseline
Safety Analysis Set

	Low Tumour Burden (N=49)	High Tumour Burden (N=15)	Other [e] (N=39)	Total (N=103)
TFR-Free Survival, N				
n (missing)	49 (0)	15 (0)	39 (0)	103 (0)
Censored n (%)	48 (98.0)	13 (86.7)	36 (92.3)	97 (94.2)
Events n (%)	1 (2.0)	2 (13.3)	3 (7.7)	6 (5.8)
Median Time to TFR Onset [a](months)	NR	NR	NR	NR
Two-sided 95% CI [b]	(NR, NR)	(NR, NR)	(NR, NR)	(NR, NR)

CI = Confidence Interval; Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; NC=Not calculable; NR=Not reached.
The time to TFR is defined as (TFR onset date - date of first Lenalidomide dose date + 1)/30.4375. Patients reporting no TFR will be censored at the date of last information available within the 6-month period. Death related to a TFR event will be considered as an event. Death unrelated to TFR will be considered as a censoring event. All times to event will be censored at 6 months after the first Lenalidomide dose date
[a] Median is based on Kaplan-Meier estimates.
[b] Two-sided Confidence interval based on the Kaplan-Meier estimates.
[c] Probability based on Kaplan-Meier estimates.
[d] The mean and median are the univariate statistics without adjusting for censoring.
[e] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
the following warning shows up: 'The likelihood ratio test for strata homogeneity is questionable since some strata have no events'
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a115_t_14_2_3_2.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 15APR2024 9:41
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.3.2
Summary of Time to Tumour Flare Reaction (TFR) Onset by Tumour Burden Status at Baseline
Safety Analysis Set

	Low Tumour Burden (N=49)	High Tumour Burden (N=15)	Other [e] (N=39)	Total (N=103)
Timepoints TFR-Free Survival probability[c]				
28 days (Cycle 1) (95% CI)	98.0 (86.4, 99.7)	93.3 (61.3, 99.0)	94.7 (80.5, 98.7)	96.1 (89.9, 98.5)
56 days (Cycle 2) (95% CI)	98.0 (86.4, 99.7)	93.3 (61.3, 99.0)	94.7 (80.5, 98.7)	96.1 (89.9, 98.5)
84 days (Cycle 3) (95% CI)	98.0 (86.4, 99.7)	93.3 (61.3, 99.0)	94.7 (80.5, 98.7)	96.1 (89.9, 98.5)
6 months estimate (95% CI)	98.0 (86.4, 99.7)	84.8 (51.2, 96.0)	91.2 (74.9, 97.1)	93.6 (86.1, 97.1)

CI = Confidence Interval; Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; NC=Not calculable; NR=Not reached.
The time to TFR is defined as (TFR onset date - date of first Lenalidomide dose date + 1)/30.4375. Patients reporting no TFR will be censored at the date of last information available within the 6-month period. Death related to a TFR event will be considered as an event. Death unrelated to TFR will be considered as a censoring event. All times to event will be censored at 6 months after the first Lenalidomide dose date
[a] Median is based on Kaplan-Meier estimates.
[b] Two-sided Confidence interval based on the Kaplan-Meier estimates.
[c] Probability based on Kaplan-Meier estimates.
[d] The mean and median are the univariate statistics without adjusting for censoring.
[e] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
the following warning shows up: 'The likelihood ratio test for strata homogeneity is questionable since some strata have no events'
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a115_t_14_2_3_2.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 15APR2024 9:41
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.3.2
Summary of Time to Tumour Flare Reaction (TFR) Onset by Tumour Burden Status at Baseline
Safety Analysis Set

	Low Tumour Burden (N=49)	High Tumour Burden (N=15)	Other [e] (N=39)	Total (N=103)
Follow-up Duration (months)				
n	49	15	39	103
Mean [d]	5.30	4.68	4.58	4.94
SD	1.556	2.285	1.996	1.860
Median [d]	6.03	6.01	6.03	6.03
Q1, Q3	5.95, 6.03	2.66, 6.03	3.02, 6.03	3.78, 6.03
Min, Max	0.33, 6.03	0.26, 6.03	0.16, 6.03	0.16, 6.03

CI = Confidence Interval; Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; NC=Not calculable; NR=Not reached.
The time to TFR is defined as (TFR onset date - date of first Lenalidomide dose date + 1)/30.4375. Patients reporting no TFR will be censored at the date of last information available within the 6-month period. Death related to a TFR event will be considered as an event. Death unrelated to TFR will be considered as a censoring event. All times to event will be censored at 6 months after the first Lenalidomide dose date
[a] Median is based on Kaplan-Meier estimates.
[b] Two-sided Confidence interval based on the Kaplan-Meier estimates.
[c] Probability based on Kaplan-Meier estimates.
[d] The mean and median are the univariate statistics without adjusting for censoring.
[e] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
the following warning shows up: 'The likelihood ratio test for strata homogeneity is questionable since some strata have no events'
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a115_t_14_2_3_2.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 15APR2024 9:41
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.4.1
Incidence of Early Death by Tumour Burden Status at Baseline
Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other [d] (N=38)	Total (N=101)
Number of Early Deaths	6	3	11	20
Cumulative Incidence of Early Death [a] %	12.5	20.0	28.9	19.8
[95% CI] [b] %	(4.7, 25.2)	(4.3, 48.1)	(15.4, 45.9)	(12.5, 28.9)
Incidence Rate of Early Death per 100 Person-Years, %	34.9	61.5	87.6	57.8
95% CI [c]	(15.7, 77.7)	(19.8, 190.7)	(48.5, 158.2)	(37.3, 89.6)

CI = Confidence Interval
[a] Defined as death occurring within 20 weeks of the initial administration of lenalidomide
[b] Clopper-Pearson is used to calculted 95% CI
[c] 95% CI for IR per 100 person-years is calculated using the method by RG Miller: IR*exp{±1.96/square root of n}.
[d] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Cross-Reference: Listing 16.2.6.1: Tumour Flare Reaction and Survival Status (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a116_t_14_2_4_1.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:39
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.4.2
Incidence of Early Death by Tumour Burden Status at Baseline
Safety Analysis Set

	Low Tumour Burden (N=49)	High Tumour Burden (N=15)	Other [d] (N=39)	Total (N=103)
Number of Early Deaths	7	3	11	21
Cumulative Incidence of Early Death [a] %	14.3	20.0	28.2	20.4
[95% CI] [b] %	(5.9, 27.2)	(4.3, 48.1)	(15.0, 44.9)	(13.1, 29.5)
Incidence Rate of Early Death per 100 Person-Years, %	40.0	61.5	85.0	59.5
95% CI [c]	(19.1, 83.9)	(19.8, 190.7)	(47.1, 153.5)	(38.8, 91.3)

CI = Confidence Interval
[a] Defined as death occurring within 20 weeks of the initial administration of lenalidomide
[b] Clopper-Pearson is used to calculted 95% CI
[c] 95% CI for IR per 100 person-years is calculated using the method by RG Miller: IR*exp{±1.96/square root of n}.
[d] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a116_t_14_2_4_2.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:39
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.5.1
Summary of Time to Early Death by Tumour Burden Status at Baseline
Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other [e] (N=38)	Total (N=101)
Early Death Free Survival, N				
n (%)	48 (100.0)	15 (100.0)	38 (100.0)	101 (100.0)
Censored n (%)	42 (87.5)	12 (80.0)	27 (71.1)	81 (80.2)
Events n (%)	6 (12.5)	3 (20.0)	11 (28.9)	20 (19.8)
Median Time to Early Death [a](months)	NR	NR	NR	NR
Two-sided 95% CI [b]	(NR, NR)	(2.7, NR)	(NR, NR)	(NR, NR)

CI = Confidence Interval, Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; NC=Not calculable; NR=Not reached; NA=Not Applicable.
The time to Early Death is defined as (Death date - date of first Lenalidomide dose date + 1)/30.4375. All times to event will be censored at 20 weeks after the first Lenalidomide dose date
[a] Median is based on Kaplan-Meier estimates.
[b] Two-sided Confidence interval based on the Kaplan-Meier estimates.
[c] Probability based on Kaplan-Meier estimates.
[d] The mean and median are the univariate statistics without adjusting for censoring.
[e] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Cross-Reference: Listing 16.2.6.1: Tumour Flare Reaction and Survival Status (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a117_t_14_2_5_1.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:39
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.5.1
Summary of Time to Early Death by Tumour Burden Status at Baseline
Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other [e] (N=38)	Total (N=101)
Timepoints Early Death Free Survival Probability [c]				
1 month estimate (95% CI)	100.0 (NC, NC)	93.3 (61.3, 99.0)	94.7 (80.6, 98.7)	97.0 (91.1, 99.0)
2 month estimate (95% CI)	93.7 (81.9, 97.9)	86.7 (56.4, 96.5)	92.1 (77.5, 97.4)	92.1 (84.8, 96.0)
3 month estimate (95% CI)	91.6 (79.2, 96.8)	80.0 (50.0, 93.1)	84.2 (68.2, 92.6)	87.1 (78.8, 92.3)
Week 20th estimate (95% CI)	87.4 (74.0, 94.1)	80.0 (NC, NC)	70.8 (53.5, 82.6)	80.0 (70.7, 86.6)

CI = Confidence Interval, Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; NC=Not calculable; NR=Not reached; NA=Not Applicable.
The time to Early Death is defined as (Death date - date of first Lenalidomide dose date + 1)/30.4375. All times to event will be censored at 20 weeks after the first Lenalidomide dose date
[a] Median is based on Kaplan-Meier estimates.
[b] Two-sided Confidence interval based on the Kaplan-Meier estimates.
[c] Probability based on Kaplan-Meier estimates.
[d] The mean and median are the univariate statistics without adjusting for censoring.
[e] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Cross-Reference: Listing 16.2.6.1: Tumour Flare Reaction and Survival Status (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a117_t_14_2_5_1.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:39
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.5.1
Summary of Time to Early Death by Tumour Burden Status at Baseline
Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other [e] (N=38)	Total (N=101)
Follow-up Duration (months)				
n	48	15	38	101
Mean [d]	4.30	3.90	3.96	4.11
SD	0.908	1.404	1.192	1.104
Median [d]	4.63	4.63	4.63	4.63
Q1, Q3	4.63, 4.63	3.35, 4.63	3.06, 4.63	4.63, 4.63
Min, Max	1.2, 4.6	0.3, 4.6	0.4, 4.6	0.3, 4.6

CI = Confidence Interval, Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; NC=Not calculable; NR=Not reached; NA=Not Applicable.
The time to Early Death is defined as (Death date - date of first Lenalidomide dose date + 1)/30.4375. All times to event will be censored at 20 weeks after the first Lenalidomide dose date
[a] Median is based on Kaplan-Meier estimates.
[b] Two-sided Confidence interval based on the Kaplan-Meier estimates.
[c] Probability based on Kaplan-Meier estimates.
[d] The mean and median are the univariate statistics without adjusting for censoring.
[e] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Cross-Reference: Listing 16.2.6.1: Tumour Flare Reaction and Survival Status (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a117_t_14_2_5_1.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:39
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.5.2
Summary of Time to Early Death by Tumour Burden Status at Baseline
Safety Analysis Set

	Low Tumour Burden (N=49)	High Tumour Burden (N=15)	Other [e] (N=39)	Total (N=103)
Early Death Free Survival, N				
n (%)	49 (100.0)	15 (100.0)	39 (100.0)	103 (100.0)
Censored n (%)	42 (85.7)	12 (80.0)	28 (71.8)	82 (79.6)
Events n (%)	7 (14.3)	3 (20.0)	11 (28.2)	21 (20.4)
Missing (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Median Time to Early Death [a](months)	NR	NR	NR	NR
Two-sided 95% CI [b]	(NR, NR)	(2.7, NR)	(NR, NR)	(NR, NR)

CI = Confidence Interval, Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; NC=Not calculable; NR=Not reached; NA=Not Applicable.
The time to Early Death is defined as (Death date - date of first Lenalidomide dose date + 1)/30.4375. All times to event will be censored at 20 weeks after the first Lenalidomide dose date
[a] Median is based on Kaplan-Meier estimates.
[b] Two-sided Confidence interval based on the Kaplan-Meier estimates.
[c] Probability based on Kaplan-Meier estimates.
[d] The mean and median are the univariate statistics without adjusting for censoring.
[e] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a117_t_14_2_5_2.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:39
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.5.2
Summary of Time to Early Death by Tumour Burden Status at Baseline
Safety Analysis Set

	Low Tumour Burden (N=49)	High Tumour Burden (N=15)	Other [e] (N=39)	Total (N=103)
Timepoints Early Death Free Survival Probability [c]				
1 month estimate (95% CI)	100.0 (NC, NC)	93.3 (61.3, 99.0)	94.9 (81.0, 98.7)	97.1 (91.2, 99.1)
2 month estimate (95% CI)	93.9 (82.2, 98.0)	86.7 (56.4, 96.5)	92.3 (78.0, 97.5)	92.2 (85.1, 96.0)
3 month estimate (95% CI)	91.8 (79.6, 96.8)	80.0 (50.0, 93.1)	84.6 (68.9, 92.8)	87.3 (79.2, 92.4)
Week 20th estimate (95% CI)	85.5 (72.0, 92.8)	80.0 (NC, NC)	71.5 (54.5, 83.1)	79.4 (70.1, 86.0)

CI = Confidence Interval, Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; NC=Not calculable; NR=Not reached; NA=Not Applicable.
The time to Early Death is defined as (Death date - date of first Lenalidomide dose date + 1)/30.4375. All times to event will be censored at 20 weeks after the first Lenalidomide dose date
[a] Median is based on Kaplan-Meier estimates.
[b] Two-sided Confidence interval based on the Kaplan-Meier estimates.
[c] Probability based on Kaplan-Meier estimates.
[d] The mean and median are the univariate statistics without adjusting for censoring.
[e] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a117_t_14_2_5_2.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:39
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.5.2
Summary of Time to Early Death by Tumour Burden Status at Baseline
Safety Analysis Set

	Low Tumour Burden (N=49)	High Tumour Burden (N=15)	Other [e] (N=39)	Total (N=103)
Follow-up Duration (months)				
n	49	15	39	103
Mean [d]	4.28	3.90	3.98	4.11
SD	0.903	1.404	1.181	1.096
Median [d]	4.63	4.63	4.63	4.63
Q1, Q3	4.63, 4.63	3.35, 4.63	3.06, 4.63	4.63, 4.63
Min, Max	1.2, 4.6	0.3, 4.6	0.4, 4.6	0.3, 4.6

CI = Confidence Interval, Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation; NC=Not calculable; NR=Not reached; NA=Not Applicable.
The time to Early Death is defined as (Death date - date of first Lenalidomide dose date + 1)/30.4375. All times to event will be censored at 20 weeks after the first Lenalidomide dose date
[a] Median is based on Kaplan-Meier estimates.
[b] Two-sided Confidence interval based on the Kaplan-Meier estimates.
[c] Probability based on Kaplan-Meier estimates.
[d] The mean and median are the univariate statistics without adjusting for censoring.
[e] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a117_t_14_2_5_2.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:39
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.6
Summary of Multivariable Analysis Using Cox Regression on Tumour Flare Reaction (TFR)
Per Protocol Analysis Set

	Univariate Analysis			Multivariable Analysis [a]		
Baseline Risk Factor	Hazard ratio	[95% CI]	p-value	Hazard ratio	[95% CI]	p-value
Age Group (<65 vs >=65)	5.76	(1.16, 28.57)	0.0320			
Sex (Female vs Male)	4.45	(0.89, 22.16)	0.0685			
History of TFR (Yes vs No)	3.89	(0.45, 33.54)	0.2170			
Tumour Burden at Baseline (High vs Low)	6.89	(0.62, 76.05)	0.1152			

References: Age Group = >=65 Years; Sex = Male; History of TFR = No; Tumour Burden at Baseline = Low; Bulky Disease at Baseline = No; ECOG Performance Status = 0.
The time to Early Death is defined as (Death date – date of first Lenalidomide dose date + 1)/30.4375. All times to event will be censored at 20 weeks after the first Lenalidomide dose date
Variables with p-value <0.20 in the univariate analysis were selected for the multivariable. Final variables were selected using a backward elimination variable-selection procedure with an elimination criterion >0.10.
[a] No variables have been retained for the multivariable analysis.
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a118_t_14_2_6_1.sas
Data Source: ADSL, ADTTE Data Extract Date: 20Feb2024 RunTime: 19MAY2024 11:55
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.6
Summary of Multivariable Analysis Using Cox Regression on Tumour Flare Reaction (TFR)
Per Protocol Analysis Set

	Univariate Analysis			Multivariable Analysis [a]		
Baseline Risk Factor	Hazard ratio	[95% CI]	p-value	Hazard ratio	[95% CI]	p-value
Bulky Disease at Baseline (Yes vs No)	1.49	(0.16, 14.33)	0.7296			
ECOG Performance Status			0.7327			
(1 vs 0)	0.43	(0.04, 4.13)				
(2+ vs 0)	1.12	(0.12, 10.81)				

References: Age Group = >=65 Years; Sex = Male; History of TFR = No; Tumour Burden at Baseline = Low; Bulky Disease at Baseline = No; ECOG Performance Status = 0.
The time to Early Death is defined as (Death date – date of first Lenalidomide dose date + 1)/30.4375. All times to event will be censored at 20 weeks after the first Lenalidomide dose date
Variables with p-value <0.20 in the univariate analysis were selected for the multivariable. Final variables were selected using a backward elimination variable-selection procedure with an elimination criterion >0.10.
[a] No variables have been retained for the multivariable analysis.
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a118_t_14_2_6_1.sas
Data Source: ADSL, ADTTE Data Extract Date: 20Feb2024 RunTime: 19MAY2024 11:55
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.7
Summary of Multivariable Analysis Using Cox Regression on Early Death
Per Protocol Analysis Set

	Univariate Analysis			Multivariable Analysis [a]		
Baseline Risk Factor	Hazard ratio	[95% CI]	p-value	Hazard ratio	[95% CI]	p-value
Age Group (<65 vs >=65)	0.59	(0.14, 2.54)	0.4764			
Sex (Female vs Male)	2.19	(0.87, 5.49)	0.0948			
History of TFR (Yes vs No)	0.91	(0.12, 6.78)	0.9244			
Tumour Burden at Baseline (High vs Low)	1.73	(0.43, 6.93)	0.4373			

References: Age Group = >=65 Years; Sex = Male; History of TFR = No; Tumour Burden at Baseline = Low; Bulky Disease at Baseline = No; ECOG Performance Status = 0.
The time to Early Death is defined as (Death date- date of first Lenalidomide dose date + 1)/30.4375. All times to event will be censored at 20 weeks after the first Lenalidomide dose date
Variables with p-value <0.20 in the univariate analysis were selected for the Multivariable. Final variables were selected using a backward elimination variable-selection procedure with an elimination criterion >0.10.
[a] No variables have been retained for the multivariable analysis.
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a119_t_14_2_7_1.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 19MAY2024 11:58
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.7
Summary of Multivariable Analysis Using Cox Regression on Early Death
Per Protocol Analysis Set

	Univariate Analysis			Multivariable Analysis [a]		
Baseline Risk Factor	Hazard ratio	[95% CI]	p-value	Hazard ratio	[95% CI]	p-value
Bulky Disease at Baseline (Yes vs No)	1.26	(0.35, 4.51)	0.7244			
ECOG Performance Status			0.9434			
(1 vs 0)	1.01	(0.27, 3.78)				
(2+ vs 0)	1.31	(0.25, 6.77)				

References: Age Group = >=65 Years; Sex = Male; History of TFR = No; Tumour Burden at Baseline = Low; Bulky Disease at Baseline = No; ECOG Performance Status = 0.
The time to Early Death is defined as (Death date- date of first Lenalidomide dose date + 1)/30.4375. All times to event will be censored at 20 weeks after the first Lenalidomide dose date
Variables with p-value <0.20 in the univariate analysis were selected for the Multivariable. Final variables were selected using a backward elimination variable-selection procedure with an elimination criterion >0.10.
[a] No variables have been retained for the multivariable analysis.
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a119_t_14_2_7_1.sas
Data Source: ADTTE Data Extract Date: 20Feb2024 RunTime: 19MAY2024 11:58
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.8.1
Tumour Flare Reaction (TFR) Summary by Tumor Burden Status at Baseline
Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other [c] (N=38)	Total (N=101)
Patients with at Least One TFR	1 (2.1)	2 (13.3)	3 (7.9)	6 (5.9)
Patients with at Least One TFR Suspected Related to Study Drug	1 (2.1)	2 (13.3)	3 (7.9)	6 (5.9)
Patients with at Least One Serious TFR	0	1 (6.7)	1 (2.6)	2 (2.0)
Patients with at Least One Serious TFR Suspected Related to Study Drug	0	1 (6.7)	1 (2.6)	2 (2.0)
Patients with at Least One CTCAE Grade 3/4 [a] TFR	0	0	1 (2.6)	1 (1.0)
Patients with at Least One CTCAE Grade 3/4 [a] TFR Suspected Related to Study Drug	0	0	1 (2.6)	1 (1.0)

Patients are counted once per category.
[a] Graded using Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Grade 3/4 and grade 5 are mutually exclusive.
[b] Defined as (date of TFR resolution - date of TFR onset+ 1)
[c] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Cross-Reference: Listing 16.2.6.1: Tumour Flare Reaction and Survival Status (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a120_t_14_2_8_1.sas
Data Source: = ADSL, ADAE, ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:40
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.8.1
Tumour Flare Reaction (TFR) Summary by Tumor Burden Status at Baseline
Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other [c] (N=38)	Total (N=101)
Patients with at Least One TFR Leading to Death	0	1 (6.7)	0	1 (1.0)
Patients with at Least One TFR Suspected Related to Study Drug Leading to Death	0	1 (6.7)	0	1 (1.0)
Patients with at Least One TFR Leading to Permanent Study Drug Discontinuation	0	0	0	0
Patients with at Least One TFR Suspected Related to Study Drug Leading to Permanent Study Drug Discontinuation	0	0	0	0

Patients are counted once per category.
[a] Graded using Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Grade 3/4 and grade 5 are mutually exclusive.
[b] Defined as (date of TFR resolution - date of TFR onset+ 1)
[c] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Cross-Reference: Listing 16.2.6.1: Tumour Flare Reaction and Survival Status (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a120_t_14_2_8_1.sas
Data Source: = ADSL, ADAE, ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:40
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.8.1
Tumour Flare Reaction (TFR) Summary by Tumor Burden Status at Baseline
Per Protocol Analysis Set

	Low Tumour Burden (N=48)	High Tumour Burden (N=15)	Other [c] (N=38)	Total (N=101)
Time to TFR Onset (days)				
n (missing)	1 (0)	2 (0)	3 (0)	6 (0)
Mean	10.0	88.5	44.3	53.3
SD	-	113.84	54.08	68.42
Median	10.0	88.5	22.0	16.0
Q1, Q3	10.0, 10.0	8.0, 169.0	5.0, 106.0	8.0, 106.0
Min, Max	10, 10	8, 169	5, 106	5, 169
Duration of TFR (days)[b]				
n (missing)	1 (0)	2 (0)	3 (0)	6 (0)
Mean	13.0	11.0	8.7	10.2
SD	-	14.14	7.09	7.96
Median	13.0	11.0	10.0	11.5
Q1, Q3	13.0, 13.0	1.0, 21.0	1.0, 15.0	1.0, 15.0
Min, Max	13, 13	1, 21	1, 15	1, 21

Patients are counted once per category.
[a] Graded using Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Grade 3/4 and grade 5 are mutually exclusive.
[b] Defined as (date of TFR resolution - date of TFR onset+ 1)
[c] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Cross-Reference: Listing 16.2.6.1: Tumour Flare Reaction and Survival Status (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a120_t_14_2_8_1.sas
Data Source: = ADSL, ADAE, ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:40
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.8.2
Tumour Flare Reaction (TFR) Summary by Tumor Burden Status at Baseline
Safety Analysis Set

	Low Tumour Burden (N=49)	High Tumour Burden (N=15)	Other [c] (N=39)	Total (N=103)
Patients with at Least One TFR	1 (2.0)	2 (13.3)	3 (7.7)	6 (5.8)
Patients with at Least One TFR Suspected Related to Study Drug	1 (2.0)	2 (13.3)	3 (7.7)	6 (5.8)
Patients with at Least One Serious TFR	0	1 (6.7)	1 (2.6)	2 (1.9)
Patients with at Least One Serious TFR Suspected Related to Study Drug	0	1 (6.7)	1 (2.6)	2 (1.9)
Patients with at Least One CTCAE Grade 3/4 [a] TFR	0	0	1 (2.6)	1 (1.0)
Patients with at Least One CTCAE Grade 3/4 [a] TFR Suspected Related to Study Drug	0	0	1 (2.6)	1 (1.0)

Patients are counted once per category.
[a] Graded using Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Grade 3/4 and grade 5 are mutually exclusive.
[b] Defined as (date of TFR resolution - date of TFR onset+ 1)
[c] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a120_t_14_2_8_2.sas
Data Source: = ADSL, ADAE, ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:40
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.8.2
Tumour Flare Reaction (TFR) Summary by Tumor Burden Status at Baseline
Safety Analysis Set

	Low Tumour Burden (N=49)	High Tumour Burden (N=15)	Other [c] (N=39)	Total (N=103)
Patients with at Least One TFR Leading to Death	0	1 (6.7)	0	1 (1.0)
Patients with at Least One TFR Suspected Related to Study Drug Leading to Death	0	1 (6.7)	0	1 (1.0)
Patients with at Least One TFR Leading to Permanent Study Drug Discontinuation	0	0	0	0
Patients with at Least One TFR Suspected Related to Study Drug Leading to Permanent Study Drug Discontinuation	0	0	0	0

Patients are counted once per category.
[a] Graded using Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Grade 3/4 and grade 5 are mutually exclusive.
[b] Defined as (date of TFR resolution - date of TFR onset+ 1)
[c] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a120_t_14_2_8_2.sas
Data Source: = ADSL, ADAE, ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:40
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.2.8.2
Tumour Flare Reaction (TFR) Summary by Tumor Burden Status at Baseline
Safety Analysis Set

	Low Tumour Burden (N=49)	High Tumour Burden (N=15)	Other [c] (N=39)	Total (N=103)
Time to TFR Onset (days)				
n (missing)	1 (0)	2 (0)	3 (0)	6 (0)
Mean	10.0	88.5	44.3	53.3
SD	-	113.84	54.08	68.42
Median	10.0	88.5	22.0	16.0
Q1, Q3	10.0, 10.0	8.0, 169.0	5.0, 106.0	8.0, 106.0
Min, Max	10, 10	8, 169	5, 106	5, 169
Duration of TFR (days)[b]				
n (missing)	1 (0)	2 (0)	3 (0)	6 (0)
Mean	13.0	11.0	8.7	10.2
SD	-	14.14	7.09	7.96
Median	13.0	11.0	10.0	11.5
Q1, Q3	13.0, 13.0	1.0, 21.0	1.0, 15.0	1.0, 15.0
Min, Max	13, 13	1, 21	1, 15	1, 21

Patients are counted once per category.
[a] Graded using Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Grade 3/4 and grade 5 are mutually exclusive.
[b] Defined as (date of TFR resolution - date of TFR onset+ 1)
[c] Patients that the High Tumour Burden were not reported as 'Y' or 'N' are categorized as the 'Other' group
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a120_t_14_2_8_2.sas
Data Source: = ADSL, ADAE, ADTTE Data Extract Date: 20Feb2024 RunTime: 06APR2024 19:40
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.1.1
Best Response During Lenalidomide Therapy
Per Protocol Analysis Set

Parameter	Total (N=101) n (%)
Patients with best response assessment performed	39 (38.6)
Best response during Lenalidomide therapy [a]	
Complete Response	12 (30.8)
Partial Response	16 (41.0)
Stable Disease	6 (15.4)
Progressive Disease	5 (12.8)
Not Evaluable	0 (0.0%)
Unknown	0 (0.0%)
Method of response assessment [a]	
CT Scan	18 (46.2)
MRI	1 (2.6)
OTHER	1 (2.6)
Pet/Ct Scan	11 (28.2)
Unknown	8 (20.5)

[a] Percentages are calculated using the number of patients who performed the best response assessment.
Cross-Reference: Listing 16.2.6.2: Best Response During Lenalidomide Therapy (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a121_t_14_3_1_1.sas
Data Source: ADRS Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:07
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.2.1.1
Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC Summary
Per Protocol Analysis Set

TEAE Categories	Total (N=101) n (%)
Patients with at Least One Related AE	10 (9.9)
Patients with at Least One Serious Related AE	4 (4.0)
Patients with at Least One CTCAE Grade 3/4 [a] Related AE	5 (5.0)
Patients with at Least One Related AE Leading to Death	3 (3.0)
Patients with at Least One Related AE Leading to Permanent Study Drug Discontinuation	2 (2.0)

Patients are counted once per category.
[a] Graded using Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Grade 3/4 and grade 5 are mutually exclusive.
Cross-reference: Listing 16.2.7.1: Adverse Events not Listed in Current EU SmPC (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a122_t_14_3_2_1_1.sas
Data Source: ADAE Data Extract Date: 20Feb2024 RunTime: 11JUL2024 21:00
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.2.1.2
Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC Summary
Safety Analysis Set

TEAE Categories	Total (N=103) n (%)
Patients with at Least One Related AE	10 (9.7)
Patients with at Least One Serious Related AE	4 (3.9)
Patients with at Least One CTCAE Grade 3/4 [a] Related AE	5 (4.9)
Patients with at Least One Related AE Leading to Death	3 (2.9)
Patients with at Least One Related AE Leading to Permanent Study Drug Discontinuation	2 (1.9)

Patients are counted once per category.
[a] Graded using Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Grade 3/4 and grade 5 are mutually exclusive.
Cross-reference: Listing 16.2.7.1: Adverse Events not Listed in Current EU SmPC (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a122_t_14_3_2_1_2.sas
Data Source: ADAE Data Extract Date: 20Feb2024 RunTime: 11JUL2024 21:00
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.2.2.1
Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC by System Organ Class and Preferred Term
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Patients With at Least One Related AE	10 (9.9)
Blood and lymphatic system disorders	3 (3.0)
Immune thrombocytopenia	1 (1.0)
Lymphadenopathy	1 (1.0)
Lymphocytosis	1 (1.0)
General disorders and administration site conditions	2 (2.0)
Death	1 (1.0)
General physical health deterioration	1 (1.0)
Immune system disorders	2 (2.0)
Graft versus host disease in gastrointestinal tract	1 (1.0)
Graft versus host disease in skin	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.7.1: Adverse Events not Listed in Current EU SmPC (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a123_t_14_3_2_2_1.sas
Data Source: ADAE Data Extract Date: 20Feb2024 RunTime: 11JUL2024 21:01
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.2.2.1
Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC by System Organ Class and Preferred Term
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Haemophagocytic lymphohistiocytosis	1 (1.0)
Nervous system disorders	2 (2.0)
Encephalopathy	1 (1.0)
Presyncope	1 (1.0)
Hepatobiliary disorders	1 (1.0)
Venoocclusive liver disease	1 (1.0)
Investigations	1 (1.0)
Glomerular filtration rate decreased	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.7.1: Adverse Events not Listed in Current EU SmPC (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a123_t_14_3_2_2_1.sas
Data Source: ADAE Data Extract Date: 20Feb2024 RunTime: 11JUL2024 21:01
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.2.2.2
Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC by System Organ Class and Preferred Term
Safety Analysis Set

System Organ Class Preferred Term [a]	Total (N=103) n (%)
Patients With at Least One Related AE	10 (9.7)
Blood and lymphatic system disorders	3 (2.9)
Immune thrombocytopenia	1 (1.0)
Lymphadenopathy	1 (1.0)
Lymphocytosis	1 (1.0)
General disorders and administration site conditions	2 (1.9)
Death	1 (1.0)
General physical health deterioration	1 (1.0)
Immune system disorders	2 (1.9)
Graft versus host disease in gastrointestinal tract	1 (1.0)
Graft versus host disease in skin	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.7.1: Adverse Events not Listed in Current EU SmPC (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a123_t_14_3_2_2_2.sas
Data Source: ADAE Data Extract Date: 20Feb2024 RunTime: 11JUL2024 21:01
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.2.2.2
Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC by System Organ Class and Preferred Term
Safety Analysis Set

System Organ Class Preferred Term [a]	Total (N=103) n (%)
Haemophagocytic lymphohistiocytosis	1 (1.0)
Nervous system disorders	2 (1.9)
Encephalopathy	1 (1.0)
Presyncope	1 (1.0)
Hepatobiliary disorders	1 (1.0)
Venoocclusive liver disease	1 (1.0)
Investigations	1 (1.0)
Glomerular filtration rate decreased	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.7.1: Adverse Events not Listed in Current EU SmPC (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a123_t_14_3_2_2_2.sas
Data Source: ADAE Data Extract Date: 20Feb2024 RunTime: 11JUL2024 21:01
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.2.3.1
Serious Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC by System Organ Class and Preferred Term
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Patients With at Least One Serious Related AE	4 (4.0)
General disorders and administration site conditions	2 (2.0)
Death	1 (1.0)
General physical health deterioration	1 (1.0)
Blood and lymphatic system disorders	1 (1.0)
Immune thrombocytopenia	1 (1.0)
Hepatobiliary disorders	1 (1.0)
Venoocclusive liver disease	1 (1.0)
Nervous system disorders	1 (1.0)
Encephalopathy	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.7.3: Serious Adverse Events not Listed in Current EU SmPC (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a124_t_14_3_2_3_1.sas
Data Source: ADAE Data Extract Date: 20Feb2024 RunTime: 11JUL2024 21:01
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.2.3.2
Serious Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC by System Organ Class and Preferred Term
Safety Analysis Set

System Organ Class Preferred Term [a]	Total (N=103) n (%)
Patients With at Least One Serious Related AE	4 (3.9)
General disorders and administration site conditions	2 (1.9)
Death	1 (1.0)
General physical health deterioration	1 (1.0)
Blood and lymphatic system disorders	1 (1.0)
Immune thrombocytopenia	1 (1.0)
Hepatobiliary disorders	1 (1.0)
Venoocclusive liver disease	1 (1.0)
Nervous system disorders	1 (1.0)
Encephalopathy	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.7.3: Serious Adverse Events not Listed in Current EU SmPC (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a124_t_14_3_2_3_2.sas
Data Source: ADAE Data Extract Date: 20Feb2024 RunTime: 11JUL2024 21:01
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.2.4.1
Grade 3/4 Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC by System Organ Class and Preferred Term
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Patients With at Least One Grade 3/4 Related AE	5 (5.0)
Nervous system disorders	2 (2.0)
Encephalopathy	1 (1.0)
Presyncope	1 (1.0)
Blood and lymphatic system disorders	1 (1.0)
Immune thrombocytopenia	1 (1.0)
Immune system disorders	1 (1.0)
Haemophagocytic lymphohistiocytosis	1 (1.0)
Investigations	1 (1.0)
Glomerular filtration rate decreased	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.7.2: Grade 3/4 Adverse Events Related to Lenalidomide and not Listed in Current EU SmPC (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a125_t_14_3_2_4_1.sas
Data Source: ADAE Data Extract Date: 20Feb2024 RunTime: 11JUL2024 21:01
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.2.4.2
Grade 3/4 Adverse Events Related to Lenalidomide and Not Listed in Current EU SmPC by System Organ Class and Preferred Term
Safety Analysis Set

System Organ Class Preferred Term [a]	Total (N=103) n (%)
Patients With at Least One Grade 3/4 Related AE	5 (4.9)
Nervous system disorders	2 (1.9)
Encephalopathy	1 (1.0)
Presyncope	1 (1.0)
Blood and lymphatic system disorders	1 (1.0)
Immune thrombocytopenia	1 (1.0)
Immune system disorders	1 (1.0)
Haemophagocytic lymphohistiocytosis	1 (1.0)
Investigations	1 (1.0)
Glomerular filtration rate decreased	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.7.2: Grade 3/4 Adverse Events Related to Lenalidomide and not Listed in Current EU SmPC (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a125_t_14_3_2_4_2.sas
Data Source: ADAE Data Extract Date: 20Feb2024 RunTime: 11JUL2024 21:01
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.2.5.1
Adverse Events Related to Lenalidomide Leading to Death and Not Listed in Current EU SmPC by System Organ Class and Preferred Term
Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Patients With at Least One Related AE Leading to Death	3 (3.0)
General disorders and administration site conditions	2 (2.0)
Death	1 (1.0)
General physical health deterioration	1 (1.0)
Hepatobiliary disorders	1 (1.0)
Venoocclusive liver disease	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Any Death reported with preferred term 'Death' corresponds to undefined death.
Cross-reference: Listing 16.2.7.4: Adverse Events not Listed in Current EU SmPC Leading to Death (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a126_t_14_3_2_5_1.sas
Data Source: ADAE Data Extract Date: 20Feb2024 RunTime: 11JUL2024 21:01
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.2.5.2
Adverse Events Related to Lenalidomide Leading to Death and Not Listed in Current EU SmPC by System Organ Class and Preferred Term
Safety Analysis Set

System Organ Class Preferred Term [a]	Total (N=103) n (%)
Patients With at Least One Related AE Leading to Death	3 (2.9)
General disorders and administration site conditions	2 (1.9)
Death	1 (1.0)
General physical health deterioration	1 (1.0)
Hepatobiliary disorders	1 (1.0)
Venoocclusive liver disease	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Any Death reported with preferred term 'Death' corresponds to undefined death.
Cross-reference: Listing 16.2.7.4: Adverse Events not Listed in Current EU SmPC Leading to Death (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a126_t_14_3_2_5_2.sas
Data Source: ADAE Data Extract Date: 20Feb2024 RunTime: 11JUL2024 21:01
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.2.6.1

Adverse Events Related to Lenalidomide Leading to Permanent Study Drug Discontinuation and Not Listed in Current EU SmPC by System Organ Class and Preferred Term

Per Protocol Analysis Set

System Organ Class Preferred Term [a]	Total (N=101) n (%)
Patients With at Least One Related AE Leading to Permanent Study Drug Discontinuation	2 (2.0)
Immune system disorders	2 (2.0)
Graft versus host disease in gastrointestinal tract	1 (1.0)
Haemophagocytic lymphohistiocytosis	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.

Cross-reference: Listing 16.2.7.5: Adverse Events not Listed in Current EU SmPC Leading to Permanent Study Drug Discontinuation (Per Protocol Analysis Set).

Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a127_t_14_3_2_6_1.sas

Data Source: ADAE Data Extract Date: 20Feb2024 RunTime: 11JUL2024 21:02

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Table 14.3.2.6.2
Adverse Events Related to Lenalidomide Leading to Permanent Study Drug Discontinuation and Not Listed in Current EU SmPC by System Organ Class and Preferred Term
Safety Analysis Set

System Organ Class Preferred Term [a]	Total (N=103) n (%)
Patients With at Least One Related AE Leading to Permanent Study Drug Discontinuation	2 (1.9)
Immune system disorders	2 (1.9)
Graft versus host disease in gastrointestinal tract	1 (1.0)
Haemophagocytic lymphohistiocytosis	1 (1.0)

[a] Coded using MedDRA version 26.0. A patient is counted only once for multiple events within preferred term/system organ class. Terms not in the MedDRA dictionary will be classified as 'Not Coded'.
Cross-reference: Listing 16.2.7.5: Adverse Events not Listed in Current EU SmPC Leading to Permanent Study Drug Discontinuation (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a127_t_14_3_2_6_2.sas
Data Source: ADAE Data Extract Date: 20Feb2024 RunTime: 11JUL2024 21:02
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.3.1
Death Summary
Per Protocol Analysis Set

Parameter	Total (N=101) n (%)
Overall number of deaths	26 (25.7)
Primary cause of death	
Atrioventricular block complete	1 (3.8)
Death	5 (19.2)
General physical health deterioration	2 (7.7)
Mantle cell lymphoma	8 (30.8)
Mantle cell lymphoma recurrent	1 (3.8)
Multiple organ dysfunction syndrome	1 (3.8)
Myocardial ischaemia	1 (3.8)
Non-hodgkin's lymphoma	2 (7.7)
Pneumonia bacterial	1 (3.8)
Respiratory failure	1 (3.8)
Sepsis	1 (3.8)
Urosepsis	1 (3.8)
Venoocclusive liver disease	1 (3.8)

[a] On treatment death is defined as a death occurring either during the course of treatment or within 28 days following the discontinuation of treatment.
Cross-reference: Listing 16.2.6.1: tumour Flare Reaction and Survival Status (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a128_t_14_3_3_1.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 17MAR2024 16:00
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.3.1
Death Summary
Per Protocol Analysis Set

Parameter	Total (N=101) n (%)
Number of deaths on treatment [a]	7 (6.9)
Primary cause of death on treatment	
Atrioventricular block complete	1 (14.3)
Mantle cell lymphoma	3 (42.9)
Myocardial ischaemia	1 (14.3)
Pneumonia bacterial	1 (14.3)
Urosepsis	1 (14.3)

[a] On treatment death is defined as a death occurring either during the course of treatment or within 28 days following the discontinuation of treatment.
Cross-reference: Listing 16.2.6.1: tumour Flare Reaction and Survival Status (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a128_t_14_3_3_1.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 17MAR2024 16:00
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.3.2.1
Early Death Summary
Per Protocol Analysis Set

Parameter	Total (N=101) n (%)
Overall number of early deaths [a]	20 (19.8)
Primary cause of early death	
Death	3 (15.0)
General physical health deterioration	2 (10.0)
Mantle cell lymphoma	7 (35.0)
Mantle cell lymphoma recurrent	1 (5.0)
Multiple organ dysfunction syndrome	1 (5.0)
Myocardial ischaemia	1 (5.0)
Non-hodgkin's lymphoma	1 (5.0)
Pneumonia bacterial	1 (5.0)
Respiratory failure	1 (5.0)
Sepsis	1 (5.0)
Urosepsis	1 (5.0)

[a] Defined as death occurring within 20 weeks of the initial administration of lenalidomide.
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a129_t_14_3_3_2_1.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:13
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.3.2.2
Early Death Summary
Safety Analysis Set

Parameter	Total (N=103) n (%)
Overall number of early deaths [a]	21 (20.4)
Primary cause of early death	
Death	3 (14.3)
General physical health deterioration	2 (9.5)
Mantle cell lymphoma	8 (38.1)
Mantle cell lymphoma recurrent	1 (4.8)
Multiple organ dysfunction syndrome	1 (4.8)
Myocardial ischaemia	1 (4.8)
Non-hodgkin's lymphoma	1 (4.8)
Pneumonia bacterial	1 (4.8)
Respiratory failure	1 (4.8)
Sepsis	1 (4.8)
Urosepsis	1 (4.8)

[a] Defined as death occurring within 20 weeks of the initial administration of lenalidomide.
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a129_t_14_3_3_2_2.sas
Data Source: ADSL Data Extract Date: 20Feb2024 RunTime: 05APR2024 12:12
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.1.1
Physical Exam at Baseline
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Baseline	
Spleen	
n (%)	4 (4.0)
Normal	3 (75.0)
Abnormal	1 (25.0)
Enlarged	0 (0.0)
Enlarged and decreased	0 (0.0)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	97 (96.0)
Liver	
n (%)	3 (3.0)
Normal	2 (66.7)
Abnormal	0 (0.0)
Enlarged	1 (33.3)
Enlarged and decreased	0 (0.0)
Enlarged and increased	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a130_t_14_3_4_1_1.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 04APR2024 21:26
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.1.1
Physical Exam at Baseline
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Enlarged and stable	0 (0.0)
Missing, n (%)	98 (97.0)
Lymph Node	
n (%)	4 (4.0)
Normal	3 (75.0)
Abnormal	1 (25.0)
Enlarged	0 (0.0)
Enlarged and decreased	0 (0.0)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	97 (96.0)
Lymph Node Location [a]	
n (%)	1 (100.0)
Axillary Lymph Node	0 (0.0)
Inguinal Lymph Node	1 (100.0)
Supraclavicular Lymph Node	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a130_t_14_3_4_1_1.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 04APR2024 21:26
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.1.1
Physical Exam at Baseline
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Upper Cervical Lymph Node	0 (0.0)
Other [b]	0 (0.0)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a130_t_14_3_4_1_1.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 04APR2024 21:26
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 01	
Spleen	
n (%)	38 (37.6)
Normal	29 (76.3)
Abnormal	2 (5.3)
Enlarged	5 (13.2)
Enlarged and decreased	2 (5.3)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	63 (62.4)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	34 (33.7)
Normal	31 (91.2)
Abnormal	0 (0.0)
Enlarged	2 (5.9)
Enlarged and decreased	1 (2.9)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	67 (66.3)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	39 (38.6)
Normal	29 (74.4)
Abnormal	3 (7.7)
Enlarged	4 (10.3)
Enlarged and decreased	1 (2.6)
Enlarged and increased	1 (2.6)
Enlarged and stable	1 (2.6)
Missing, n (%)	62 (61.4)
Lymph Node Location [a]	
n (%)	10 (100.0)
Axillary Lymph Node	3 (30.0)
Inguinal Lymph Node	3 (30.0)
Supraclavicular Lymph Node	0 (0.0)
Upper Cervical Lymph Node	0 (0.0)
Other [b]	3 (30.0)
Missing, n (%)	1 (10.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 02	
Spleen	
n (%)	36 (35.6)
Normal	29 (80.6)
Abnormal	2 (5.6)
Enlarged	3 (8.3)
Enlarged and decreased	1 (2.8)
Enlarged and increased	1 (2.8)
Enlarged and stable	0 (0.0)
Missing, n (%)	65 (64.4)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	33 (32.7)
Normal	30 (90.9)
Abnormal	2 (6.1)
Enlarged	1 (3.0)
Enlarged and decreased	0 (0.0)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	68 (67.3)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	35 (34.7)
Normal	27 (77.1)
Abnormal	2 (5.7)
Enlarged	2 (5.7)
Enlarged and decreased	3 (8.6)
Enlarged and increased	0 (0.0)
Enlarged and stable	1 (2.9)
Missing, n (%)	66 (65.3)
Lymph Node Location [a]	
n (%)	8 (100.0)
Axillary Lymph Node	1 (12.5)
Inguinal Lymph Node	3 (37.5)
Supraclavicular Lymph Node	0 (0.0)
Upper Cervical Lymph Node	0 (0.0)
Other [b]	4 (50.0)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 03	
Spleen	
n (%)	32 (31.7)
Normal	27 (84.4)
Abnormal	2 (6.3)
Enlarged	2 (6.3)
Enlarged and decreased	1 (3.1)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	69 (68.3)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	30 (29.7)
Normal	29 (96.7)
Abnormal	0 (0.0)
Enlarged	1 (3.3)
Enlarged and decreased	0 (0.0)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	71 (70.3)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	35 (34.7)
Normal	27 (77.1)
Abnormal	1 (2.9)
Enlarged	2 (5.7)
Enlarged and decreased	4 (11.4)
Enlarged and increased	0 (0.0)
Enlarged and stable	1 (2.9)
Missing, n (%)	66 (65.3)
Lymph Node Location [a]	
n (%)	8 (100.0)
Axillary Lymph Node	1 (12.5)
Inguinal Lymph Node	2 (25.0)
Supraclavicular Lymph Node	1 (12.5)
Upper Cervical Lymph Node	0 (0.0)
Other [b]	4 (50.0)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 04	
Spleen	
n (%)	30 (29.7)
Normal	27 (90.0)
Abnormal	1 (3.3)
Enlarged	1 (3.3)
Enlarged and decreased	1 (3.3)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	71 (70.3)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	28 (27.7)
Normal	28 (100.0)
Abnormal	0 (0.0)
Enlarged	0 (0.0)
Enlarged and decreased	0 (0.0)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	73 (72.3)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	32 (31.7)
Normal	23 (71.9)
Abnormal	2 (6.3)
Enlarged	3 (9.4)
Enlarged and decreased	3 (9.4)
Enlarged and increased	0 (0.0)
Enlarged and stable	1 (3.1)
Missing, n (%)	69 (68.3)
Lymph Node Location [a]	
n (%)	9 (100.0)
Axillary Lymph Node	2 (22.2)
Inguinal Lymph Node	3 (33.3)
Supraclavicular Lymph Node	0 (0.0)
Upper Cervical Lymph Node	1 (11.1)
Other [b]	3 (33.3)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 05	
Spleen	
n (%)	25 (24.8)
Normal	22 (88.0)
Abnormal	1 (4.0)
Enlarged	2 (8.0)
Enlarged and decreased	0 (0.0)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	76 (75.2)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	24 (23.8)
Normal	24 (100.0)
Abnormal	0 (0.0)
Enlarged	0 (0.0)
Enlarged and decreased	0 (0.0)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	77 (76.2)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	27 (26.7)
Normal	21 (77.8)
Abnormal	1 (3.7)
Enlarged	2 (7.4)
Enlarged and decreased	3 (11.1)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	74 (73.3)
Lymph Node Location [a]	
n (%)	6 (100.0)
Axillary Lymph Node	1 (16.7)
Inguinal Lymph Node	2 (33.3)
Supraclavicular Lymph Node	0 (0.0)
Upper Cervical Lymph Node	1 (16.7)
Other [b]	2 (33.3)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 06	
Spleen	
n (%)	18 (17.8)
Normal	15 (83.3)
Abnormal	1 (5.6)
Enlarged	2 (11.1)
Enlarged and decreased	0 (0.0)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	83 (82.2)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	17 (16.8)
Normal	17 (100.0)
Abnormal	0 (0.0)
Enlarged	0 (0.0)
Enlarged and decreased	0 (0.0)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	84 (83.2)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	18 (17.8)
Normal	12 (66.7)
Abnormal	0 (0.0)
Enlarged	1 (5.6)
Enlarged and decreased	1 (5.6)
Enlarged and increased	3 (16.7)
Enlarged and stable	1 (5.6)
Missing, n (%)	83 (82.2)
Lymph Node Location [a]	
n (%)	6 (100.0)
Axillary Lymph Node	1 (16.7)
Inguinal Lymph Node	1 (16.7)
Supraclavicular Lymph Node	0 (0.0)
Upper Cervical Lymph Node	1 (16.7)
Other [b]	3 (50.0)
Missing, n (%)	0 (0.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 07	
Spleen	
n (%)	2 (2.0)
Normal	2 (100.0)
Abnormal	0 (0.0)
Enlarged	0 (0.0)
Enlarged and decreased	0 (0.0)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	99 (98.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	2 (2.0)
Normal	2 (100.0)
Abnormal	0 (0.0)
Enlarged	0 (0.0)
Enlarged and decreased	0 (0.0)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	99 (98.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	2 (2.0)
Normal	2 (100.0)
Abnormal	0 (0.0)
Enlarged	0 (0.0)
Enlarged and decreased	0 (0.0)
Enlarged and increased	0 (0.0)
Enlarged and stable	0 (0.0)
Missing, n (%)	99 (98.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 08	
Spleen	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)
Lymph Node Location [a]	-
n (%)	0 (0.0)
Axillary Lymph Node	-
Inguinal Lymph Node	-
Supraclavicular Lymph Node	-
Upper Cervical Lymph Node	-
Other	-
Missing, n (%)	-

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 09	
Spleen	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)
Lymph Node Location [a]	-
n (%)	0 (0.0)
Axillary Lymph Node	-
Inguinal Lymph Node	-
Supraclavicular Lymph Node	-
Upper Cervical Lymph Node	-
Other	-
Missing, n (%)	-

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 10	
Spleen	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)
Lymph Node Location [a]	-
n (%)	0 (0.0)
Axillary Lymph Node	-
Inguinal Lymph Node	-
Supraclavicular Lymph Node	-
Upper Cervical Lymph Node	-
Other	-
Missing, n (%)	-

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 11	
Spleen	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)
Lymph Node Location [a]	-
n (%)	0 (0.0)
Axillary Lymph Node	-
Inguinal Lymph Node	-
Supraclavicular Lymph Node	-
Upper Cervical Lymph Node	-
Other	-
Missing, n (%)	-

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 12	
Spleen	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)
Lymph Node Location [a]	-
n (%)	0 (0.0)
Axillary Lymph Node	-
Inguinal Lymph Node	-
Supraclavicular Lymph Node	-
Upper Cervical Lymph Node	-
Other	-
Missing, n (%)	-

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 13	
Spleen	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)
Lymph Node Location [a]	-
n (%)	0 (0.0)
Axillary Lymph Node	-
Inguinal Lymph Node	-
Supraclavicular Lymph Node	-
Upper Cervical Lymph Node	-
Other	-
Missing, n (%)	-

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 14	
Spleen	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)
Lymph Node Location [a]	-
n (%)	0 (0.0)
Axillary Lymph Node	-
Inguinal Lymph Node	-
Supraclavicular Lymph Node	-
Upper Cervical Lymph Node	-
Other	-
Missing, n (%)	-

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 15	
Spleen	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)
Lymph Node Location [a]	-
n (%)	0 (0.0)
Axillary Lymph Node	-
Inguinal Lymph Node	-
Supraclavicular Lymph Node	-
Upper Cervical Lymph Node	-
Other	-
Missing, n (%)	-

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 16	
Spleen	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)
Lymph Node Location [a]	-
n (%)	0 (0.0)
Axillary Lymph Node	-
Inguinal Lymph Node	-
Supraclavicular Lymph Node	-
Upper Cervical Lymph Node	-
Other	-
Missing, n (%)	-

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Visit 17	
Spleen	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Liver	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
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Table 14.3.4.1.2
Physical Exam by Visit
Per Protocol Analysis Set

Visit Statistics	Total (N=101) n (%)
Lymph Node	
n (%)	0 (0.0)
Normal	-
Abnormal	-
Enlarged	-
Enlarged and decreased	-
Enlarged and increased	-
Enlarged and stable	-
Missing, n (%)	101 (100.0)
Lymph Node Location [a]	-
n (%)	0 (0.0)
Axillary Lymph Node	-
Inguinal Lymph Node	-
Supraclavicular Lymph Node	-
Upper Cervical Lymph Node	-
Other	-
Missing, n (%)	-

Max=Maximum; Min=Minimum; Q1=First quartile; Q3=Third quartile; SD=Standard deviation.
[a] Percentages are calculated using the number of patients who reported abnormal or enlarged results for lymph nodes.
[b] Other examinations include locations other than the spleen, liver and lymphadenopathy that may be present in any region of the body.
Cross-reference: 16.2.8.1: Physical Exam (Per Protocol Analysis Set).
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a131_t_14_3_4_1_2.sas
Data Source: ADPE Data Extract Date: 20Feb2024 RunTime: 07APR2024 11:11
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Circulating Tumor Cells (10^9/L)	
BASELINE	
n	2
Mean	0.0
SD	0.00
Median	0.0
Q1, Q3	0.0, 0.0
Min, Max	0, 0
VISIT 01	
n	1
Mean	0.0
SD	-
Median	0.0
Q1, Q3	0.0, 0.0
Min, Max	0, 0

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	2
Mean	6.3
SD	8.91
Median	6.3
Q1, Q3	0.0, 12.6
Min, Max	0, 13
VISIT 03	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	1
Mean	2.5
SD	-
Median	2.5
Q1, Q3	2.5, 2.5
Min, Max	3, 3
VISIT 05	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 07	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 09	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 11	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 13	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 15	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Hemoglobin (g/L)	
BASELINE	
n	90
Mean	119.0
SD	22.83
Median	121.0
Q1, Q3	102.0, 136.0
Min, Max	70, 167
VISIT 01	
n	73
Mean	117.4
SD	19.70
Median	117.0
Q1, Q3	107.0, 132.0
Min, Max	74, 158

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	59
Mean	117.2
SD	20.04
Median	120.0
Q1, Q3	102.0, 131.0
Min, Max	64, 150
VISIT 03	
n	57
Mean	121.6
SD	16.98
Median	122.0
Q1, Q3	111.0, 136.0
Min, Max	85, 155

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	55
Mean	118.6
SD	17.33
Median	118.0
Q1, Q3	106.0, 130.4
Min, Max	71, 152
VISIT 05	
n	52
Mean	119.1
SD	16.58
Median	119.0
Q1, Q3	108.0, 131.5
Min, Max	82, 152

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	38
Mean	116.1
SD	16.87
Median	117.5
Q1, Q3	104.0, 126.0
Min, Max	78, 147
VISIT 07	
n	5
Mean	120.2
SD	15.71
Median	116.0
Q1, Q3	109.0, 120.0
Min, Max	109, 147

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	2
Mean	102.5
SD	7.78
Median	102.5
Q1, Q3	97.0, 108.0
Min, Max	97, 108
VISIT 09	
n	1
Mean	99.0
SD	-
Median	99.0
Q1, Q3	99.0, 99.0
Min, Max	99, 99

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	1
Mean	87.0
SD	-
Median	87.0
Q1, Q3	87.0, 87.0
Min, Max	87, 87
VISIT 11	
n	1
Mean	87.0
SD	-
Median	87.0
Q1, Q3	87.0, 87.0
Min, Max	87, 87

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	1
Mean	91.0
SD	-
Median	91.0
Q1, Q3	91.0, 91.0
Min, Max	91, 91
VISIT 13	
n	1
Mean	93.0
SD	-
Median	93.0
Q1, Q3	93.0, 93.0
Min, Max	93, 93

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	1
Mean	100.0
SD	-
Median	100.0
Q1, Q3	100.0, 100.0
Min, Max	100, 100
VISIT 15	
n	1
Mean	105.0
SD	-
Median	105.0
Q1, Q3	105.0, 105.0
Min, Max	105, 105

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	1
Mean	125.0
SD	-
Median	125.0
Q1, Q3	125.0, 125.0
Min, Max	125, 125

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Lymphocytes (10^9/L)	
BASELINE	
n	78
Mean	5.1
SD	14.89
Median	1.4
Q1, Q3	0.7, 2.3
Min, Max	0, 86
VISIT 01	
n	59
Mean	2.9
SD	7.84
Median	1.1
Q1, Q3	0.7, 2.0
Min, Max	0, 54

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	48
Mean	4.0
SD	12.25
Median	1.1
Q1, Q3	0.7, 1.9
Min, Max	0, 83
VISIT 03	
n	48
Mean	3.4
SD	13.00
Median	1.4
Q1, Q3	0.7, 2.1
Min, Max	0, 91

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	47
Mean	2.5
SD	6.22
Median	1.2
Q1, Q3	0.8, 2.0
Min, Max	0, 43
VISIT 05	
n	43
Mean	5.7
SD	18.10
Median	1.2
Q1, Q3	0.8, 1.7
Min, Max	0, 105

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	29
Mean	4.3
SD	15.36
Median	1.1
Q1, Q3	0.7, 2.4
Min, Max	0, 84
VISIT 07	
n	5
Mean	1.6
SD	1.12
Median	1.1
Q1, Q3	0.9, 2.1
Min, Max	1, 3

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	2
Mean	1.9
SD	1.94
Median	1.9
Q1, Q3	0.5, 3.2
Min, Max	1, 3
VISIT 09	
n	1
Mean	3.2
SD	-
Median	3.2
Q1, Q3	3.2, 3.2
Min, Max	3, 3

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	1
Mean	2.3
SD	-
Median	2.3
Q1, Q3	2.3, 2.3
Min, Max	2, 2
VISIT 11	
n	1
Mean	2.7
SD	-
Median	2.7
Q1, Q3	2.7, 2.7
Min, Max	3, 3

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	1
Mean	1.7
SD	-
Median	1.7
Q1, Q3	1.7, 1.7
Min, Max	2, 2
VISIT 13	
n	1
Mean	2.7
SD	-
Median	2.7
Q1, Q3	2.7, 2.7
Min, Max	3, 3

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	1
Mean	2.4
SD	-
Median	2.4
Q1, Q3	2.4, 2.4
Min, Max	2, 2
VISIT 15	
n	1
Mean	2.3
SD	-
Median	2.3
Q1, Q3	2.3, 2.3
Min, Max	2, 2

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	1
Mean	2.5
SD	-
Median	2.5
Q1, Q3	2.5, 2.5
Min, Max	2, 2

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Neutrophils (10^9/L)	
BASELINE	
n	82
Mean	3.8
SD	2.64
Median	3.3
Q1, Q3	2.2, 4.8
Min, Max	0, 17
VISIT 01	
n	63
Mean	2.9
SD	2.62
Median	2.2
Q1, Q3	1.3, 3.8
Min, Max	0, 18

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	52
Mean	2.7
SD	1.93
Median	2.3
Q1, Q3	1.5, 3.2
Min, Max	0, 10
VISIT 03	
n	49
Mean	2.4
SD	1.70
Median	2.0
Q1, Q3	1.2, 2.9
Min, Max	0, 9

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	50
Mean	2.6
SD	2.24
Median	2.0
Q1, Q3	1.2, 2.9
Min, Max	0, 14
VISIT 05	
n	45
Mean	3.0
SD	2.80
Median	2.0
Q1, Q3	1.3, 3.5
Min, Max	0, 16

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	31
Mean	2.3
SD	2.42
Median	1.8
Q1, Q3	1.1, 3.0
Min, Max	0, 14
VISIT 07	
n	5
Mean	1.9
SD	1.28
Median	1.8
Q1, Q3	0.7, 2.8
Min, Max	1, 4

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	2
Mean	3.3
SD	4.31
Median	3.3
Q1, Q3	0.3, 6.4
Min, Max	0, 6
VISIT 09	
n	1
Mean	3.0
SD	-
Median	3.0
Q1, Q3	3.0, 3.0
Min, Max	3, 3

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	1
Mean	3.5
SD	-
Median	3.5
Q1, Q3	3.5, 3.5
Min, Max	4, 4
VISIT 11	
n	1
Mean	2.6
SD	-
Median	2.6
Q1, Q3	2.6, 2.6
Min, Max	3, 3

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	1
Mean	4.3
SD	-
Median	4.3
Q1, Q3	4.3, 4.3
Min, Max	4, 4
VISIT 13	
n	1
Mean	4.0
SD	-
Median	4.0
Q1, Q3	4.0, 4.0
Min, Max	4, 4

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	1
Mean	2.3
SD	-
Median	2.3
Q1, Q3	2.3, 2.3
Min, Max	2, 2
VISIT 15	
n	1
Mean	2.2
SD	-
Median	2.2
Q1, Q3	2.2, 2.2
Min, Max	2, 2

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	1
Mean	2.3
SD	-
Median	2.3
Q1, Q3	2.3, 2.3
Min, Max	2, 2

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Platelets (10^9/L)	
BASELINE	
n	89
Mean	162.3
SD	83.39
Median	169.0
Q1, Q3	93.0, 219.0
Min, Max	10, 352
VISIT 01	
n	73
Mean	166.5
SD	80.90
Median	172.0
Q1, Q3	119.0, 207.0
Min, Max	5, 401

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	59
Mean	167.3
SD	80.40
Median	162.0
Q1, Q3	118.0, 209.0
Min, Max	11, 399
VISIT 03	
n	57
Mean	172.1
SD	72.16
Median	171.0
Q1, Q3	120.0, 219.0
Min, Max	39, 364

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	55
Mean	166.8
SD	90.23
Median	166.0
Q1, Q3	106.0, 207.0
Min, Max	17, 531
VISIT 05	
n	52
Mean	162.2
SD	73.03
Median	165.5
Q1, Q3	105.0, 230.5
Min, Max	34, 293

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	38
Mean	154.1
SD	91.32
Median	133.0
Q1, Q3	93.0, 191.0
Min, Max	12, 464
VISIT 07	
n	5
Mean	206.2
SD	149.17
Median	150.0
Q1, Q3	97.0, 262.0
Min, Max	81, 441

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	2
Mean	207.5
SD	94.05
Median	207.5
Q1, Q3	141.0, 274.0
Min, Max	141, 274
VISIT 09	
n	1
Mean	372.0
SD	-
Median	372.0
Q1, Q3	372.0, 372.0
Min, Max	372, 372

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	1
Mean	293.0
SD	-
Median	293.0
Q1, Q3	293.0, 293.0
Min, Max	293, 293
VISIT 11	
n	1
Mean	370.0
SD	-
Median	370.0
Q1, Q3	370.0, 370.0
Min, Max	370, 370

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	1
Mean	376.0
SD	-
Median	376.0
Q1, Q3	376.0, 376.0
Min, Max	376, 376
VISIT 13	
n	1
Mean	297.0
SD	-
Median	297.0
Q1, Q3	297.0, 297.0
Min, Max	297, 297

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	1
Mean	240.0
SD	-
Median	240.0
Q1, Q3	240.0, 240.0
Min, Max	240, 240
VISIT 15	
n	1
Mean	144.0
SD	-
Median	144.0
Q1, Q3	144.0, 144.0
Min, Max	144, 144

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	1
Mean	253.0
SD	-
Median	253.0
Q1, Q3	253.0, 253.0
Min, Max	253, 253

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Leukocytes (10^9/L)	
BASELINE	
n	90
Mean	11.9
SD	24.05
Median	6.0
Q1, Q3	4.7, 8.4
Min, Max	1, 185
VISIT 01	
n	73
Mean	8.1
SD	14.06
Median	5.0
Q1, Q3	3.7, 6.6
Min, Max	1, 101

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	59
Mean	7.5
SD	11.57
Median	4.6
Q1, Q3	3.7, 6.8
Min, Max	2, 85
VISIT 03	
n	57
Mean	6.7
SD	12.63
Median	4.5
Q1, Q3	3.1, 6.0
Min, Max	1, 96

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	55
Mean	6.4
SD	7.54
Median	4.4
Q1, Q3	3.0, 6.1
Min, Max	1, 45
VISIT 05	
n	52
Mean	9.7
SD	18.02
Median	4.3
Q1, Q3	2.9, 6.9
Min, Max	1, 109

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	38
Mean	11.3
SD	22.95
Median	4.3
Q1, Q3	3.0, 6.1
Min, Max	1, 90
VISIT 07	
n	5
Mean	4.3
SD	2.51
Median	4.5
Q1, Q3	2.7, 4.6
Min, Max	1, 8

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	2
Mean	6.1
SD	7.00
Median	6.1
Q1, Q3	1.1, 11.0
Min, Max	1, 11
VISIT 09	
n	1
Mean	7.5
SD	-
Median	7.5
Q1, Q3	7.5, 7.5
Min, Max	8, 8

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	1
Mean	6.6
SD	-
Median	6.6
Q1, Q3	6.6, 6.6
Min, Max	7, 7
VISIT 11	
n	1
Mean	6.7
SD	-
Median	6.7
Q1, Q3	6.7, 6.7
Min, Max	7, 7

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	1
Mean	6.8
SD	-
Median	6.8
Q1, Q3	6.8, 6.8
Min, Max	7, 7
VISIT 13	
n	1
Mean	7.6
SD	-
Median	7.6
Q1, Q3	7.6, 7.6
Min, Max	8, 8

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	1
Mean	5.9
SD	-
Median	5.9
Q1, Q3	5.9, 5.9
Min, Max	6, 6
VISIT 15	
n	1
Mean	5.1
SD	-
Median	5.1
Q1, Q3	5.1, 5.1
Min, Max	5, 5

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.2
Hematology Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	1
Mean	6.2
SD	-
Median	6.2
Q1, Q3	6.2, 6.2
Min, Max	6, 6

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a132_t_14_3_4_2.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:23
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Alanine Aminotransferase (U/L)	
BASELINE	
n	80
Mean	25.8
SD	43.40
Median	17.0
Q1, Q3	11.5, 23.0
Min, Max	3, 381
VISIT 01	
n	60
Mean	25.7
SD	21.33
Median	20.0
Q1, Q3	12.5, 30.5
Min, Max	8, 133

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	46
Mean	29.3
SD	46.95
Median	18.0
Q1, Q3	12.8, 32.0
Min, Max	5, 321
VISIT 03	
n	46
Mean	24.5
SD	22.33
Median	19.0
Q1, Q3	14.0, 26.0
Min, Max	8, 129

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	45
Mean	24.1
SD	19.42
Median	18.0
Q1, Q3	14.0, 28.0
Min, Max	6, 120
VISIT 05	
n	43
Mean	25.6
SD	21.18
Median	20.0
Q1, Q3	14.0, 31.0
Min, Max	8, 130

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	31
Mean	20.5
SD	10.69
Median	17.0
Q1, Q3	13.0, 27.0
Min, Max	8, 46
VISIT 07	
n	4
Mean	17.0
SD	3.37
Median	17.0
Q1, Q3	14.5, 19.5
Min, Max	13, 21

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	1
Mean	16.0
SD	-
Median	16.0
Q1, Q3	16.0, 16.0
Min, Max	16, 16
VISIT 09	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 11	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 13	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 15	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Albumin (g/L)	
BASELINE	
n	52
Mean	39.8
SD	5.23
Median	40.3
Q1, Q3	35.5, 43.8
Min, Max	25, 50
VISIT 01	
n	27
Mean	37.2
SD	5.93
Median	38.1
Q1, Q3	34.0, 42.0
Min, Max	24, 46

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	19
Mean	38.7
SD	7.08
Median	39.9
Q1, Q3	35.0, 43.0
Min, Max	22, 51
VISIT 03	
n	21
Mean	40.6
SD	6.11
Median	41.0
Q1, Q3	37.0, 45.0
Min, Max	22, 50

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	18
Mean	38.8
SD	5.62
Median	38.4
Q1, Q3	36.0, 44.0
Min, Max	23, 47
VISIT 05	
n	18
Mean	39.2
SD	4.93
Median	40.8
Q1, Q3	36.0, 43.0
Min, Max	26, 46

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	15
Mean	39.0
SD	4.73
Median	40.0
Q1, Q3	35.0, 42.0
Min, Max	28, 48
VISIT 07	
n	5
Mean	38.0
SD	6.37
Median	37.0
Q1, Q3	36.3, 42.8
Min, Max	29, 45

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	1
Mean	44.0
SD	-
Median	44.0
Q1, Q3	44.0, 44.0
Min, Max	44, 44
VISIT 09	
n	1
Mean	29.3
SD	-
Median	29.3
Q1, Q3	29.3, 29.3
Min, Max	29, 29

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 11	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 13	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 15	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Aspartate Aminotransferase (U/L)	
BASELINE	
n	75
Mean	26.0
SD	25.77
Median	21.0
Q1, Q3	15.0, 30.0
Min, Max	7, 226
VISIT 01	
n	57
Mean	22.1
SD	10.27
Median	20.0
Q1, Q3	16.0, 26.0
Min, Max	8, 57

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	44
Mean	26.5
SD	37.83
Median	19.0
Q1, Q3	14.5, 26.0
Min, Max	9, 263
VISIT 03	
n	44
Mean	22.0
SD	10.05
Median	22.0
Q1, Q3	15.5, 24.0
Min, Max	9, 67

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	43
Mean	20.4
SD	7.12
Median	21.0
Q1, Q3	15.0, 25.0
Min, Max	7, 36
VISIT 05	
n	38
Mean	28.3
SD	36.32
Median	21.0
Q1, Q3	16.0, 26.0
Min, Max	10, 240

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	29
Mean	19.5
SD	5.46
Median	19.0
Q1, Q3	16.0, 22.0
Min, Max	9, 32
VISIT 07	
n	4
Mean	21.8
SD	4.50
Median	20.5
Q1, Q3	18.5, 25.0
Min, Max	18, 28

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	1
Mean	17.0
SD	-
Median	17.0
Q1, Q3	17.0, 17.0
Min, Max	17, 17
VISIT 09	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 11	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 13	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 15	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Bilirubin (umol/L)	
BASELINE	
n	67
Mean	11.2
SD	10.15
Median	9.7
Q1, Q3	6.8, 13.7
Min, Max	3, 84
VISIT 01	
n	49
Mean	10.6
SD	6.25
Median	8.6
Q1, Q3	6.8, 13.7
Min, Max	3, 33

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	38
Mean	11.0
SD	6.75
Median	8.6
Q1, Q3	6.8, 12.0
Min, Max	4, 31
VISIT 03	
n	37
Mean	10.4
SD	4.37
Median	10.3
Q1, Q3	7.2, 12.5
Min, Max	3, 22

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	36
Mean	10.0
SD	5.08
Median	9.1
Q1, Q3	5.6, 13.2
Min, Max	3, 22
VISIT 05	
n	30
Mean	11.9
SD	7.21
Median	11.8
Q1, Q3	6.2, 14.7
Min, Max	4, 39

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	23
Mean	11.4
SD	5.11
Median	10.3
Q1, Q3	6.8, 15.4
Min, Max	4, 22
VISIT 07	
n	3
Mean	16.9
SD	13.71
Median	11.3
Q1, Q3	6.8, 32.5
Min, Max	7, 32

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	1
Mean	5.1
SD	-
Median	5.1
Q1, Q3	5.1, 5.1
Min, Max	5, 5
VISIT 09	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 11	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 13	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	1
Mean	3.6
SD	-
Median	3.6
Q1, Q3	3.6, 3.6
Min, Max	4, 4
VISIT 15	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
C Reactive Protein (mg/L)	
BASELINE	
n	58
Mean	23.0
SD	36.51
Median	10.7
Q1, Q3	4.0, 28.0
Min, Max	0, 244
VISIT 01	
n	39
Mean	26.1
SD	43.37
Median	8.5
Q1, Q3	2.9, 28.0
Min, Max	1, 224

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	32
Mean	35.0
SD	69.66
Median	5.0
Q1, Q3	2.0, 27.1
Min, Max	0, 330
VISIT 03	
n	29
Mean	15.4
SD	27.57
Median	4.0
Q1, Q3	2.0, 14.2
Min, Max	0, 133

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	26
Mean	13.4
SD	22.08
Median	4.7
Q1, Q3	1.7, 13.0
Min, Max	0, 83
VISIT 05	
n	30
Mean	19.0
SD	33.65
Median	7.0
Q1, Q3	2.9, 19.9
Min, Max	0, 171

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	24
Mean	12.5
SD	18.24
Median	5.1
Q1, Q3	1.8, 15.5
Min, Max	0, 71
VISIT 07	
n	3
Mean	13.6
SD	20.26
Median	2.9
Q1, Q3	1.0, 37.0
Min, Max	1, 37

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	1
Mean	48.6
SD	-
Median	48.6
Q1, Q3	48.6, 48.6
Min, Max	49, 49
VISIT 09	
n	1
Mean	44.1
SD	-
Median	44.1
Q1, Q3	44.1, 44.1
Min, Max	44, 44

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	1
Mean	28.4
SD	-
Median	28.4
Q1, Q3	28.4, 28.4
Min, Max	28, 28
VISIT 11	
n	1
Mean	53.3
SD	-
Median	53.3
Q1, Q3	53.3, 53.3
Min, Max	53, 53

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	1
Mean	92.8
SD	-
Median	92.8
Q1, Q3	92.8, 92.8
Min, Max	93, 93
VISIT 13	
n	1
Mean	21.2
SD	-
Median	21.2
Q1, Q3	21.2, 21.2
Min, Max	21, 21

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	1
Mean	3.5
SD	-
Median	3.5
Q1, Q3	3.5, 3.5
Min, Max	4, 4
VISIT 15	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	1
Mean	57.0
SD	-
Median	57.0
Q1, Q3	57.0, 57.0
Min, Max	57, 57

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Calcium (mmol/L)	
BASELINE	
n	67
Mean	2.3
SD	0.13
Median	2.3
Q1, Q3	2.2, 2.4
Min, Max	2, 3
VISIT 01	
n	45
Mean	2.3
SD	0.22
Median	2.3
Q1, Q3	2.2, 2.4
Min, Max	1, 3

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	36
Mean	2.3
SD	0.16
Median	2.3
Q1, Q3	2.2, 2.4
Min, Max	2, 3
VISIT 03	
n	38
Mean	2.3
SD	0.11
Median	2.3
Q1, Q3	2.2, 2.4
Min, Max	2, 3

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	32
Mean	2.3
SD	0.12
Median	2.3
Q1, Q3	2.2, 2.4
Min, Max	2, 3
VISIT 05	
n	31
Mean	2.3
SD	0.18
Median	2.3
Q1, Q3	2.2, 2.4
Min, Max	2, 3

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	24
Mean	2.3
SD	0.11
Median	2.2
Q1, Q3	2.2, 2.3
Min, Max	2, 3
VISIT 07	
n	5
Mean	2.2
SD	0.17
Median	2.2
Q1, Q3	2.1, 2.3
Min, Max	2, 2

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	1
Mean	2.0
SD	-
Median	2.0
Q1, Q3	2.0, 2.0
Min, Max	2, 2
VISIT 09	
n	1
Mean	2.1
SD	-
Median	2.1
Q1, Q3	2.1, 2.1
Min, Max	2, 2

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 11	
n	1
Mean	2.1
SD	-
Median	2.1
Q1, Q3	2.1, 2.1
Min, Max	2, 2

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 13	
n	1
Mean	2.1
SD	-
Median	2.1
Q1, Q3	2.1, 2.1
Min, Max	2, 2

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 15	
n	1
Mean	2.1
SD	-
Median	2.1
Q1, Q3	2.1, 2.1
Min, Max	2, 2

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	1
Mean	2.3
SD	-
Median	2.3
Q1, Q3	2.3, 2.3
Min, Max	2, 2

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Creatinine (umol/L)	
BASELINE	
n	89
Mean	98.3
SD	34.27
Median	92.0
Q1, Q3	74.3, 114.9
Min, Max	48, 267
VISIT 01	
n	68
Mean	100.4
SD	33.17
Median	91.1
Q1, Q3	79.6, 115.9
Min, Max	48, 222

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	51
Mean	99.7
SD	32.25
Median	97.4
Q1, Q3	79.6, 111.4
Min, Max	10, 193
VISIT 03	
n	50
Mean	101.2
SD	26.87
Median	101.3
Q1, Q3	79.6, 119.3
Min, Max	59, 176

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	48
Mean	101.9
SD	32.07
Median	97.2
Q1, Q3	80.7, 111.8
Min, Max	52, 236
VISIT 05	
n	48
Mean	108.4
SD	51.69
Median	100.8
Q1, Q3	79.6, 114.0
Min, Max	58, 398

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	35
Mean	109.1
SD	33.16
Median	106.1
Q1, Q3	89.3, 123.8
Min, Max	57, 229
VISIT 07	
n	5
Mean	95.5
SD	14.62
Median	98.1
Q1, Q3	81.3, 106.1
Min, Max	80, 112

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	2
Mean	98.1
SD	23.75
Median	98.1
Q1, Q3	81.3, 114.9
Min, Max	81, 115
VISIT 09	
n	1
Mean	84.9
SD	-
Median	84.9
Q1, Q3	84.9, 84.9
Min, Max	85, 85

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	1
Mean	94.6
SD	-
Median	94.6
Q1, Q3	94.6, 94.6
Min, Max	95, 95
VISIT 11	
n	1
Mean	87.5
SD	-
Median	87.5
Q1, Q3	87.5, 87.5
Min, Max	88, 88

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	1
Mean	103.4
SD	-
Median	103.4
Q1, Q3	103.4, 103.4
Min, Max	103, 103
VISIT 13	
n	1
Mean	94.6
SD	-
Median	94.6
Q1, Q3	94.6, 94.6
Min, Max	95, 95

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	1
Mean	87.5
SD	-
Median	87.5
Q1, Q3	87.5, 87.5
Min, Max	88, 88
VISIT 15	
n	1
Mean	87.5
SD	-
Median	87.5
Q1, Q3	87.5, 87.5
Min, Max	88, 88

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	1
Mean	93.7
SD	-
Median	93.7
Q1, Q3	93.7, 93.7
Min, Max	94, 94

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Creatinine Clearance (mL/s)	
BASELINE	
n	18
Mean	1.0
SD	0.33
Median	1.0
Q1, Q3	0.8, 1.3
Min, Max	0, 1
VISIT 01	
n	9
Mean	1.0
SD	0.22
Median	1.0
Q1, Q3	0.9, 1.2
Min, Max	1, 1

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	6
Mean	1.0
SD	0.16
Median	1.0
Q1, Q3	0.9, 1.2
Min, Max	1, 1
VISIT 03	
n	6
Mean	0.9
SD	0.19
Median	1.0
Q1, Q3	0.8, 1.0
Min, Max	1, 1

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	8
Mean	1.0
SD	0.33
Median	1.0
Q1, Q3	0.8, 1.2
Min, Max	0, 1
VISIT 05	
n	8
Mean	1.0
SD	0.42
Median	0.9
Q1, Q3	0.8, 1.3
Min, Max	0, 2

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	7
Mean	0.9
SD	0.27
Median	0.9
Q1, Q3	0.9, 1.2
Min, Max	0, 1
VISIT 07	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 09	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 11	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 13	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 15	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Direct Bilirubin (umol/L)	
BASELINE	
n	25
Mean	7.2
SD	14.64
Median	3.9
Q1, Q3	3.1, 5.3
Min, Max	2, 77
VISIT 01	
n	18
Mean	4.8
SD	3.98
Median	3.5
Q1, Q3	2.7, 5.1
Min, Max	2, 18

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	18
Mean	5.3
SD	4.22
Median	3.4
Q1, Q3	3.1, 5.1
Min, Max	2, 18
VISIT 03	
n	15
Mean	4.1
SD	1.29
Median	4.1
Q1, Q3	3.2, 5.1
Min, Max	2, 6

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	10
Mean	3.6
SD	0.99
Median	3.4
Q1, Q3	2.9, 4.7
Min, Max	2, 5
VISIT 05	
n	10
Mean	7.7
SD	9.36
Median	5.1
Q1, Q3	4.0, 5.1
Min, Max	3, 34

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	6
Mean	4.9
SD	1.75
Median	5.1
Q1, Q3	3.8, 6.4
Min, Max	2, 7
VISIT 07	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 09	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 11	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 13	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 15	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
GFR from Creatinine Adjusted for BSA (mL/min/1.73m2)	
BASELINE	
n	23
Mean	68.4
SD	18.83
Median	72.0
Q1, Q3	53.0, 84.0
Min, Max	40, 102
VISIT 01	
n	21
Mean	67.6
SD	19.83
Median	65.0
Q1, Q3	52.5, 79.0
Min, Max	38, 102

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	18
Mean	61.4
SD	21.94
Median	61.5
Q1, Q3	50.8, 80.8
Min, Max	10, 94
VISIT 03	
n	15
Mean	61.3
SD	19.55
Median	62.0
Q1, Q3	40.0, 80.8
Min, Max	37, 92

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	15
Mean	66.6
SD	16.85
Median	63.0
Q1, Q3	59.0, 80.0
Min, Max	37, 94
VISIT 05	
n	16
Mean	62.9
SD	18.65
Median	61.4
Q1, Q3	47.0, 80.0
Min, Max	35, 94

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	10
Mean	59.2
SD	17.77
Median	58.8
Q1, Q3	46.0, 76.0
Min, Max	36, 90
VISIT 07	
n	1
Mean	81.0
SD	-
Median	81.0
Q1, Q3	81.0, 81.0
Min, Max	81, 81

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 09	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 11	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 13	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 15	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Glomerular Filtration Rate Adj for BSA (mL/min/1.73m2)	
BASELINE	
n	18
Mean	63.2
SD	20.40
Median	61.8
Q1, Q3	47.0, 79.0
Min, Max	33, 101
VISIT 01	
n	18
Mean	64.9
SD	25.38
Median	60.7
Q1, Q3	44.9, 77.0
Min, Max	32, 122

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	14
Mean	59.9
SD	17.26
Median	58.4
Q1, Q3	47.0, 70.0
Min, Max	29, 98
VISIT 03	
n	14
Mean	57.5
SD	14.17
Median	53.1
Q1, Q3	49.0, 63.0
Min, Max	39, 95

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	10
Mean	59.0
SD	19.48
Median	55.5
Q1, Q3	43.5, 79.0
Min, Max	32, 88
VISIT 05	
n	11
Mean	50.9
SD	20.68
Median	48.7
Q1, Q3	39.2, 60.0
Min, Max	13, 91

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	8
Mean	49.8
SD	9.60
Median	51.5
Q1, Q3	42.6, 55.0
Min, Max	35, 65
VISIT 07	
n	1
Mean	53.6
SD	-
Median	53.6
Q1, Q3	53.6, 53.6
Min, Max	54, 54

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 09	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 11	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 13	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 15	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Glucose (mmol/L)	
BASELINE	
n	62
Mean	5.6
SD	1.36
Median	5.4
Q1, Q3	4.9, 5.9
Min, Max	3, 10
VISIT 01	
n	40
Mean	5.8
SD	1.71
Median	5.3
Q1, Q3	5.0, 5.9
Min, Max	3, 12

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	31
Mean	5.3
SD	1.48
Median	5.3
Q1, Q3	4.6, 5.9
Min, Max	1, 9
VISIT 03	
n	33
Mean	5.5
SD	1.31
Median	5.5
Q1, Q3	4.7, 6.0
Min, Max	1, 9

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	29
Mean	5.8
SD	1.46
Median	5.4
Q1, Q3	5.1, 6.2
Min, Max	4, 12
VISIT 05	
n	29
Mean	5.5
SD	1.31
Median	5.4
Q1, Q3	4.9, 6.1
Min, Max	2, 8

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	23
Mean	5.9
SD	1.58
Median	5.6
Q1, Q3	4.9, 6.9
Min, Max	4, 11
VISIT 07	
n	4
Mean	5.3
SD	0.26
Median	5.2
Q1, Q3	5.1, 5.4
Min, Max	5, 6

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	2
Mean	5.6
SD	0.59
Median	5.6
Q1, Q3	5.2, 6.0
Min, Max	5, 6
VISIT 09	
n	1
Mean	6.4
SD	-
Median	6.4
Q1, Q3	6.4, 6.4
Min, Max	6, 6

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 11	
n	1
Mean	5.6
SD	-
Median	5.6
Q1, Q3	5.6, 5.6
Min, Max	6, 6

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	1
Mean	10.3
SD	-
Median	10.3
Q1, Q3	10.3, 10.3
Min, Max	10, 10
VISIT 13	
n	1
Mean	6.0
SD	-
Median	6.0
Q1, Q3	6.0, 6.0
Min, Max	6, 6

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
Prepared by ICON Commercialisation & Outcomes, Biostatistics and Medical Writing

Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	1
Mean	5.0
SD	-
Median	5.0
Q1, Q3	5.0, 5.0
Min, Max	5, 5
VISIT 15	
n	1
Mean	5.6
SD	-
Median	5.6
Q1, Q3	5.6, 5.6
Min, Max	6, 6

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	1
Mean	6.3
SD	-
Median	6.3
Q1, Q3	6.3, 6.3
Min, Max	6, 6

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Lactate Dehydrogenase (U/L)	
BASELINE	
n	79
Mean	314.2
SD	170.05
Median	262.0
Q1, Q3	189.0, 388.0
Min, Max	119, 961
VISIT 01	
n	54
Mean	334.8
SD	406.77
Median	223.5
Q1, Q3	181.0, 334.0
Min, Max	69, 3041

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	40
Mean	319.3
SD	479.75
Median	200.5
Q1, Q3	153.2, 311.0
Min, Max	102, 3168
VISIT 03	
n	45
Mean	264.6
SD	133.21
Median	212.0
Q1, Q3	175.0, 296.0
Min, Max	123, 640

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	40
Mean	278.3
SD	174.46
Median	221.5
Q1, Q3	175.5, 354.0
Min, Max	119, 1016
VISIT 05	
n	38
Mean	294.8
SD	396.93
Median	206.0
Q1, Q3	164.0, 259.0
Min, Max	109, 2566

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	30
Mean	275.2
SD	263.96
Median	212.0
Q1, Q3	162.0, 285.0
Min, Max	105, 1591
VISIT 07	
n	5
Mean	162.4
SD	25.13
Median	155.0
Q1, Q3	141.0, 178.0
Min, Max	140, 198

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	2
Mean	130.5
SD	9.19
Median	130.5
Q1, Q3	124.0, 137.0
Min, Max	124, 137
VISIT 09	
n	1
Mean	147.0
SD	-
Median	147.0
Q1, Q3	147.0, 147.0
Min, Max	147, 147

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	1
Mean	119.0
SD	-
Median	119.0
Q1, Q3	119.0, 119.0
Min, Max	119, 119
VISIT 11	
n	1
Mean	139.0
SD	-
Median	139.0
Q1, Q3	139.0, 139.0
Min, Max	139, 139

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 13	
n	1
Mean	227.0
SD	-
Median	227.0
Q1, Q3	227.0, 227.0
Min, Max	227, 227

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 15	
n	1
Mean	132.0
SD	-
Median	132.0
Q1, Q3	132.0, 132.0
Min, Max	132, 132

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	1
Mean	126.0
SD	-
Median	126.0
Q1, Q3	126.0, 126.0
Min, Max	126, 126

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Phosphate (mmol/L)	
BASELINE	
n	22
Mean	1.1
SD	0.21
Median	1.1
Q1, Q3	0.9, 1.2
Min, Max	1, 2
VISIT 01	
n	14
Mean	1.0
SD	0.20
Median	1.0
Q1, Q3	0.9, 1.1
Min, Max	1, 2

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	11
Mean	1.0
SD	0.19
Median	1.1
Q1, Q3	0.9, 1.2
Min, Max	1, 1
VISIT 03	
n	12
Mean	1.0
SD	0.17
Median	1.0
Q1, Q3	1.0, 1.1
Min, Max	1, 1

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	12
Mean	1.0
SD	0.14
Median	1.0
Q1, Q3	0.9, 1.1
Min, Max	1, 1
VISIT 05	
n	10
Mean	1.1
SD	0.21
Median	1.2
Q1, Q3	1.0, 1.3
Min, Max	1, 1

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	7
Mean	1.1
SD	0.19
Median	1.1
Q1, Q3	1.0, 1.2
Min, Max	1, 1
VISIT 07	
n	1
Mean	0.9
SD	-
Median	0.9
Q1, Q3	0.9, 0.9
Min, Max	1, 1

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 09	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 11	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 13	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-
VISIT 15	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	0
Mean	-
SD	-
Median	-
Q1, Q3	-
Min, Max	-

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Potassium (mmol/L)	
BASELINE	
n	74
Mean	4.3
SD	0.49
Median	4.3
Q1, Q3	4.0, 4.6
Min, Max	3, 6
VISIT 01	
n	56
Mean	4.4
SD	0.85
Median	4.2
Q1, Q3	4.0, 4.7
Min, Max	3, 9

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	43
Mean	4.2
SD	0.53
Median	4.1
Q1, Q3	3.9, 4.4
Min, Max	3, 6
VISIT 03	
n	42
Mean	4.3
SD	0.58
Median	4.2
Q1, Q3	4.0, 4.7
Min, Max	3, 6

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	39
Mean	4.2
SD	0.53
Median	4.2
Q1, Q3	4.0, 4.5
Min, Max	3, 6
VISIT 05	
n	36
Mean	4.2
SD	0.54
Median	4.2
Q1, Q3	3.9, 4.5
Min, Max	3, 6

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	29
Mean	4.1
SD	0.53
Median	4.1
Q1, Q3	3.8, 4.4
Min, Max	3, 6
VISIT 07	
n	5
Mean	4.3
SD	0.40
Median	4.3
Q1, Q3	4.0, 4.7
Min, Max	4, 5

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	2
Mean	4.3
SD	0.01
Median	4.3
Q1, Q3	4.3, 4.3
Min, Max	4, 4
VISIT 09	
n	1
Mean	4.9
SD	-
Median	4.9
Q1, Q3	4.9, 4.9
Min, Max	5, 5

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	1
Mean	4.0
SD	-
Median	4.0
Q1, Q3	4.0, 4.0
Min, Max	4, 4
VISIT 11	
n	1
Mean	4.7
SD	-
Median	4.7
Q1, Q3	4.7, 4.7
Min, Max	5, 5

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	1
Mean	4.4
SD	-
Median	4.4
Q1, Q3	4.4, 4.4
Min, Max	4, 4
VISIT 13	
n	1
Mean	4.6
SD	-
Median	4.6
Q1, Q3	4.6, 4.6
Min, Max	5, 5

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	1
Mean	4.0
SD	-
Median	4.0
Q1, Q3	4.0, 4.0
Min, Max	4, 4
VISIT 15	
n	1
Mean	4.1
SD	-
Median	4.1
Q1, Q3	4.1, 4.1
Min, Max	4, 4

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	1
Mean	4.5
SD	-
Median	4.5
Q1, Q3	4.5, 4.5
Min, Max	5, 5

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
Sodium (mmol/L)	
BASELINE	
n	75
Mean	140.2
SD	2.66
Median	141.0
Q1, Q3	139.0, 142.0
Min, Max	133, 145
VISIT 01	
n	55
Mean	140.3
SD	4.01
Median	141.0
Q1, Q3	138.0, 143.0
Min, Max	129, 151

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
Data Source: = ADLB Data Extract Date: 20Feb2024 RunTime: 06APR2024 20:31
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 02	
n	42
Mean	140.9
SD	3.03
Median	142.0
Q1, Q3	139.0, 143.0
Min, Max	134, 147
VISIT 03	
n	40
Mean	140.9
SD	2.57
Median	142.0
Q1, Q3	139.0, 142.5
Min, Max	134, 148

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 04	
n	38
Mean	141.3
SD	2.28
Median	141.5
Q1, Q3	139.0, 143.0
Min, Max	137, 145
VISIT 05	
n	35
Mean	141.2
SD	2.71
Median	141.0
Q1, Q3	140.0, 143.0
Min, Max	136, 148

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 06	
n	26
Mean	141.0
SD	2.79
Median	141.0
Q1, Q3	139.0, 143.0
Min, Max	135, 146
VISIT 07	
n	5
Mean	140.4
SD	3.13
Median	141.0
Q1, Q3	141.0, 142.0
Min, Max	135, 143

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 08	
n	2
Mean	141.0
SD	2.83
Median	141.0
Q1, Q3	139.0, 143.0
Min, Max	139, 143
VISIT 09	
n	1
Mean	142.0
SD	-
Median	142.0
Q1, Q3	142.0, 142.0
Min, Max	142, 142

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 10	
n	1
Mean	141.0
SD	-
Median	141.0
Q1, Q3	141.0, 141.0
Min, Max	141, 141
VISIT 11	
n	1
Mean	145.0
SD	-
Median	145.0
Q1, Q3	145.0, 145.0
Min, Max	145, 145

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 12	
n	1
Mean	141.0
SD	-
Median	141.0
Q1, Q3	141.0, 141.0
Min, Max	141, 141
VISIT 13	
n	1
Mean	138.0
SD	-
Median	138.0
Q1, Q3	138.0, 138.0
Min, Max	138, 138

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 14	
n	1
Mean	141.0
SD	-
Median	141.0
Q1, Q3	141.0, 141.0
Min, Max	141, 141
VISIT 15	
n	1
Mean	141.0
SD	-
Median	141.0
Q1, Q3	141.0, 141.0
Min, Max	141, 141

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
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Table 14.3.4.3
Biochemistry Results by Visit
Per Protocol Analysis Set

Lab Test Visit Statistics	Total (N=101)
VISIT 16	
n	1
Mean	140.0
SD	-
Median	140.0
Q1, Q3	140.0, 140.0
Min, Max	140, 140

SD=Standard Deviation, Q1=First Quartile, Q3=Third Quartile, Min=Minimum, Max=Maximum, NC=Not Calculable.
Cross-reference: listing 16.2.8.2: Laboratory Data (Per Protocol Analysis Set)
Program Path: /opt/sas/data/sas_ico/sas_ico_bmw/celgene/mcl005/2024_02_20/01_TLFs/saspgm/a133_t_14_3_4_3.sas
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APPENDIX 1.7 Listings

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Approved v1.0 930231036 1.0

APPENDIX 1.7 Listings

- Listings

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